REMARKS

The Office Action rejected claim 23 under 35 U.S.C. §112, second paragraph, as indefinite with respect to the use of the term "optionally", applicants have deleted this term as suggested. Accordingly, this rejection should be withdrawn.

Claims 18 and 19 were objected to under 37CFR 1.75(c). These claims have been canceled. Thus, this objection no longer applies.

Claim 27 has been rejected under 35 U.S.C. §112, first paragraph as only being enabled for treating schizophrenia and Parkinson's Disease. This claim has been amended to delete all other uses. Accordingly, this rejection should be withdrawn.

Submitted herewith is a copy of the English Translation that was submitted on September 9, 2003 in the parent provisional application, and a copy of the postcard acknowledging receipt thereof on September 12, 2003.

Since there are no outstanding rejections or objections, a Notice of Allowance with respect to claims 1-17, 20-23 and 27 is respectfully solicited.

Respectfully submitted,

Dated: August 30, 2007

Martin L. Katz, Reg. No. 25,011
Wood, Phillips, Katz, Clark & Mortimer
Citigroup Center, Suite 3800
500 West Madison Street
Chicago, Illinois 60661
(312) 876-2110

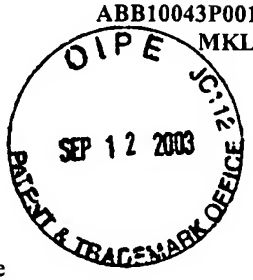
CERTIFICATE OF MAILING

I hereby certify that this Paper is being deposited with the United States Postal Service with sufficient postage at First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450 on **August 30, 2007**.

Rachel Burke

THE UNITED STATES PATENT OFFICE IS REQUESTED TO IMPRESS ITS STAMP ON THIS CARD AND PLACE SAME IN THE OUT-GOING MAIL TO SHOW THE FOLLOWING PAPERS HAVE BEEN RECEIVED

ABB10043P0010US
MKL/bjw



TRANSMITTAL OF DOCUMENTS

1) Petition for Extension of Time
2) Copy of Notice to File Missing Parts
3) Response to Notice to File Missing Parts of Application
4) Provisional Application for Patent Cover Sheet
5) Copy of English Language Translation of German Applicatoin
6) Check for $410.00 – Filing fee for Petition for Extension of Time
7) Check for $50.00 – Filing fee for Response to Notice to File Missing Parts of Appln.
8) This return postcard for:

U.S. Patent Application Serial No. 60/462,782
Inventor: Braje, et al
Filed: 04/14/2003

September 9, 2003

WOOD, PHILLIPS, KATZ, CLARK & MORTIMER

PETITION FOR EXTENSION OF TIME		Docket No.:	ABB10043P0010US
Serial No.:	60/462,782	Filing Date:	April 14, 2003
Group Art Unit:	N/A	Examiner:	N/A
Applicant(s):	Braje, et al.		
Invention:	N-[(Piperazinly)hetary]arylsufonamide Compounds		

Commissioner For Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

Applicant(s) hereby petition(s) under the provisions of 37 C.F.R. §1.136(a) to extend the period for filing a response to the Office Action of June 5, 2003 in the above-identified application for the period required to make the attached Response timely.

Extension Fee For Response Within:	**First Month**	**Second Month**	**Third Month**	**Fourth Month**
Large Entity:	☐ $110.00	☒ $410.00	☐ $930.00	☐ $1,450.00
Small Entity:	☐ $55.00	☐ $205.00	☐ $465.00	☐ $725.00

☒ A check in the amount of **410.00** to cover the extension fee is enclosed.

☐ Charge $_____ to Deposit Account No. 23-0785.

☒ The Commissioner is hereby authorized to charge any additional fees which may be required to this application under 37 C.F.R. §1.17, or credit any overpayment, to Deposit Account No. 23-0785. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

By _____
Martin L. Katz, Reg. No. 25,011

WOOD, PHILLIPS, KATZ, CLARK & MORTIMER
Citicorp Center, Suite 3800
500 West Madison Street
Chicago, Illinois 60661-2511
312/876-1800

CERTIFICATE OF MAILING

I hereby certify that this document and fee (if applicable) is being deposited with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450 on **September 9, 2003**.

_____
Rebecca J. Willis

RESPONSE TO NOTICE TO FILE MISSING PARTS OF APPLICATION		Docket No.:	ABB10043P0010US
Applicant(s):	Braje, et al.		
Serial No.:	60/462,782	Filing Date:	April 14, 2003
Group Art Unit:	N/A	Examiner:	N/A
Invention:	N-[(Piperazinly)hetary]arylsufonamide Compounds		

Mail Stop Missing Parts
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

Transmitted herewith in response to the Formalities Letter dated 06/05/2003 are:

- ☒ Executed declaration or oath for this application.
- ☒ Return copy of the Notice to File Missing Parts of Application.
- ☒ Other: English Translation and Petition for Extenion of Time
- ☐ A check in the amount of $50.00 to cover the filing fee.
- ☐ Charge $_ to Deposit Account No. 23-0785.
- ☒ The Commissioner is hereby authorized to charge any additional fees which may be required to this application under 37 C.F.R. §1.15-§1.17, or credit any overpayment, to Deposit Account No. 23-0785. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

By _____
Martin L. Katz, Reg. No. 25,011

WOOD, PHILLIPS, KATZ, CLARK & MORTIMER
Citicorp Center, Suite 3800
500 West Madison Street
Chicago, Illinois 60661-2511
312/876-1800

CERTIFICATE OF MAILING

I hereby certify that this document and fee (if applicable) is being deposited with the United States Postal Service with sufficient postage at First Class Mail in an envelope addressed to: Mail Stop Missing Parts, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on 9/9 /03.

_____
Rebecca J. Willis

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING/RECEIPT DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NUMBER
60/462,782	04/14/2003	Wilfried M. Braje	ABB10043P0010US

CONFIRMATION NO. 2491

32116
WOOD, PHILLIPS, KATZ, CLARK & MORTIMER
500 W. MADISON STREET
SUITE 3800
CHICAGO, IL 60661

FORMALITIES LETTER

OC000000010188012

Date Mailed: 06/05/2003

NOTICE TO FILE MISSING PARTS OF PROVISIONAL APPLICATION

FILED UNDER 37 CFR 1.53(c)

Filing Date Granted

An application number and filing date have been accorded to this provisional application. The items indicated below, however, are missing. Applicant is given **TWO MONTHS** from the date of this Notice within which to file all required items and pay any fees required below to avoid abandonment. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

- To avoid abandonment, a late filing fee or oath or declaration surcharge as set forth in 37 CFR 1.16(l) of $50 for a non-small entity, must be submitted with the missing items identified in this letter.
- The provisional application cover sheet under 37 CFR 1.51(c)(1), which may be an application data sheet (37 CFR 1.76), is required identifying:
  - either city and state or city and foreign country of the residence of each inventor.

SUMMARY OF FEES DUE:

Total additional fee(s) required for this application is **$50** for a Large Entity

- **$50** Late oath or declaration Surcharge.

A copy of this notice MUST be returned with the reply.

M. Tran

Customer Service Center
Initial Patent Examination Division (703) 308-1202
PART 2 - COPY TO BE RETURNED WITH RESPONSE

PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a **PROVISIONAL APPLICATION FOR PATENT** under 37 CFR 1.53(c)

Attorney Docket No:	ABB10043P0010US

INVENTOR(S)/APPLICANT(S)

Given Name (first and middle [if any])	Family Name or Surname	Residence (City and either State or Foreign Country)
Wilfried M. Andreas Wilfried	Braje Haupt Lubisch	31737 Rinteln, Germany 68723 Schwetzingen, Germany 69115 Heidelberg, Germany

☒ Additional inventors are being named on the separately numbered sheets attached hereto.

TITLE OF THE INVENTION (280 characters maximum)

N-[(Piperazinyl)hetaryl]arylsulfonamide Compounds

CORRESPONDENCE ADDRESS

Direct all correspondence to:
WOOD, PHILLIPS, KATZ,
CLARK & MORTIMER
Citicorp Center, Suite 3800
500 West Madison Street
Chicago, Illinois 60661-2511
(312) 876-1800 (phone)
(312) 876-2020 (facsimile)

Customer Number
(32116)
and/or Bar Code Label:

ENCLOSED APPLICATION PARTS *(check all that apply)*

☒	Specification *Number of Pages*	65	☐ CD(s)		☐ Application Data Sheet (37 CFR 1.76)
☐	Drawing(s) *Number of Sheets*		☒	Other (specify): 16 claims; 1 page Abstract	

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT *(check one)*

☐ Applicant claims small entity status (See 37 CFR 1.27.)
☒ A check in the amount of $____ is enclosed to cover the filing fee.
☒ The Commissioner is hereby authorized to charge the filing fee, deficiencies in the filing fee, or credit any overpayment to Deposit Account No. 23-0785. A duplicate copy of this sheet is enclosed.

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

☒ No.
☐ Yes, the name of the U.S. Government agency and the Government contract number are:_____

Respectfully submitted,

Signature _____ Date September 9, 2003

Martin L. Katz, Reg. No. 25,010

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT
Send To: Box Provisional Application, Commissioner for Patents, Washington, D.C. 20231

PTO/SB/16 (2-98)
Approved for use through 01/31/2001. OMB 0651-0037
Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PROVISIONAL APPLICATION COVER SHEET
Additional Page

Attorney Docket No: ABB10043P0010US	Type a plus sign (+) inside this box → [+]

INVENTOR(S)/APPLICANT(S)		
Given Name (first and middle [if any])	Family or Surname	Residence (city and either State or Foreign Country)
Roland	Grandel	69221 Dossenheim, Germany
Karla	Drescher	69221 Dossenheim, Germany
Herve	Geneste	67141 Neuhofen, Germany
Liliane	Unger	67065 Ludwigshafen, Germany
Daryl R.	Sauer	Trevor, Wisconsin, USA

UNITED STATES PATENT AND TRADEMARK OFFICE

I, Susan ANTHONY BA, ACIS,

Director of RWS Group plc, of Europa House, Marsham Way, Gerrards Cross, Buckinghamshire, England declare;

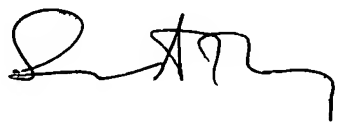
1. That I am a citizen of the United Kingdom of Great Britain and Northern Ireland.

2. That the translator responsible for the attached translation is well acquainted with the German and English languages.

3. That the attached is, to the best of RWS Group plc knowledge and belief, a true translation into the English language of the specification in German filed with the application for a patent in the U.S.A. on

under the number

4. That I believe that all statements made herein of my own knowledge are true and that all statements made on information and belief are true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the patent application in the United States of America or any patent issuing thereon.



For and on behalf of RWS Group plc

The 22nd day of July 2003

N-[(Piperazinyl)hetaryl]arylsulfonamide compounds

Description

The present invention relates to novel N-[(piperazinyl)hetaryl]arylsulfonamide compounds. The compounds possess valuable therapeutic properties and are suitable, in particular, for treating diseases which respond to modulation of the dopamine D_3 receptor.

Neurons obtain their information by way of G protein-coupled receptors, inter alia. A large number of substances exert their effect by way of these receptors. One of them is dopamine. Confirmed findings exist with regard to the presence of dopamine and its physiological function as a neurotransmitter. Disturbances in the dopaminergic transmitter system result in diseases of the central nervous system which include, for example, schizophrenia, depression and Parkinson's disease. These diseases, and others, are treated with drugs which interact with the dopamine receptors.

Up until 1990, two subtypes of dopamine receptor had been clearly defined pharmacologically, namely the D_1 and D_2 receptors. More recently, a third subtype was found, namely the D_3 receptor which appears to mediate some effects of antipsychotics and antiparkinsonians (J.C. Schwartz et al., The Dopamine D_3 Receptor as a Target for Antipsychotics, in Novel Antipsychotic Drugs, H.Y. Meltzer, Ed. Raven Press, New York 1992, pages 135-144; M. Dooley et al., Drugs and Aging 1998, 12, 495-514, J.N. Joyce, Pharmacology and Therapeutics 2001, 90, pp. 231-59 "The Dopamine D_3 Receptor as a Therapeutic Target for Antipsychotic and Antiparkinsonian Drugs").

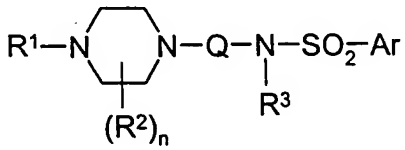
Since then, the dopamine receptors have been divided into two families. On the one hand, there is the D_2 group, consisting of D_2, D_3 and D_4 receptors, and, on the other hand, the D_1 group, consisting of D_1 and D_5 receptors. Whereas D_1 and D_2 receptors are widely distributed, D_3 receptors appear to be expressed regioselectively. Thus, these receptors are preferentially to be found in the limbic system and the projection regions of the mesolimbic dopamine system, especially in the nucleus accumbens, but also in other regions, such as the amygdala. Because of this comparatively regioselective expression, D_3 receptors are regarded as being a target having few side-effects and it is assumed that while a selective D_3 ligand would have the properties of known antipsychotics, it would not have their dopamine D_2 receptor-mediated neurological side-effects (P. Sokoloff et al., Localization and Function of the D_3 Dopamine Receptor, Arzneim. Forsch./Drug Res. 42(1), 224 (1992); P. Sokoloff et al.

Molecular Cloning and Characterization of a Novel Dopamine Receptor (D_3) as a Target for Neuroleptics, Nature, 347, 146 (1990)).

Compounds having an affinity for the dopamine D_3 receptor have been described in the prior art on various occasions, e.g. in WO 96/02519, WO 96/02520, WO 96/02249, WO 96/02246 and DE 10131543 and WO 99/02503. Some of these compounds possess high affinities for the dopamine D_3 receptor. They have therefore been proposed as being suitable for treating diseases of the central nervous system. Some of the compounds described in these publications possess a piperazinylhetaryl structure.

The invention is based on the object of providing compounds which act as selective dopamine D_3 receptor ligands.

This object is achieved by means of N-[(piperazinyl)hetaryl]arylsulfonamide compounds of the general formula I



(I)

in which

Q is a bivalent, 6-membered heteroaromatic radical which possesses 1 or 2 N atoms as ring members and which optionally carries one or two substituents R^a which is/are selected, independently of each other, from halogen, CN, NO_2, CO_2R^4, COR^5, C_1-C_4-alkyl and C_1-C_4-haloalkyl;

Ar is phenyl or a 6-membered heteroaromatic radical which possesses 1 or 2 N atoms as ring members and which optionally carries one or two substituents R^b, which is/are selected from halogen, NO_2, CN, CO_2R^4, COR^5, C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_6-cycloalkyl, C_3-C_6-cycloalkyl-C_1-C_4-alkyl and C_1-C_4-haloalkyl, with it also being possible for two radicals R^b which are bonded to adjacent C atoms of Ar to be together C_3-C_4-alkylene;

n is 0, 1 or 2;

R^1 is hydrogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_3-C_6-cycloalkyl, C_3-C_6-cycloalkyl-C_1-C_4-alkyl, C_1-C_4-hydroxyalkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_3-C_4-alkenyl or C_3-C_4-alkynyl;

R^2 is C_1-C_4-alkyl or, together with R^1, is C_2-C_5-alkylene or, in the case of n = 2, the two radicals R^2 can together be C_1-C_4-alkylene;

R^3 is hydrogen or C_1-C_4-alkyl;

R^4 is C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_2-C_4-alkenyl C_3-C_6-cycloalkyl, C_3-C_6-cycloalkyl-C_1-C_4-alkyl, phenyl or benzyl; and

R^5 is hydrogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_2-C_4-alkenyl C_3-C_6-cycloalkyl, C_3-C_6-cycloalkyl-C_1-C_4-alkyl, phenyl or benzyl;

the N-oxides thereof and the physiologically tolerated acid addition salts of these compounds.

These compounds have not previously been described, with the exception of 4-methyl-N-[6-(4-methylpiperazin-1-yl)pyridin-3-yl)benzenesulfonamide and 4-chloro-N-[6-(4-methylpiperazin-1-yl)pyridin-3-yl)benzenesulfonamide, which are offered for sale by Ambinter, Paris, as test substances for exploratory libraries.

The present invention therefore relates to N-[(piperazinyl)hetaryl]arylsulfonamide compounds of the general formula I, to their N-oxides and to their physiologically tolerated acid addition salts, with the exception of the compounds 4-methyl-N-[6-(4-methylpiperazin-1-yl)pyridin-3-yl)benzenesulfonamide and 4-chloro-N-[6-(4-methylpiperazin-1-yl)pyridin-3-yl)benzenesulfonamide.

The present invention also relates to the use of N-[(piperazinyl)hetaryl]arylsulfonamide compounds of the general formula I, of their N-oxides and of their acid addition salts for producing a pharmaceutical composition for treating diseases which respond to the influence of dopamine-D_3 receptor antagonists or agonists.

The diseases which respond to the influence of dopamine D_3 receptor antagonists or agonists include, in particular, disturbances and diseases of the central nervous system, in particular affective disturbances, neurotic disturbances, stress disturbances and somatoform disturbances and psychoses, especially schizophrenia and depression and, in addition, disturbances of kidney function, in particular kidney function disturbances which are caused by diabetes mellitus (see WO 00/67847).

According to the invention, at least one compound of the general formula I having the meanings mentioned at the outset is used for treating the abovementioned indications. Provided the compounds of the formula I possess one or more centers of asymmetry, it is also possible to use enantiomeric mixtures, in particular racemates, diastereomeric mixtures and tautomeric mixtures, preferably, however, the respective essentially pure enantiomers, diastereomers and tautomers.

It is likewise possible to use physiologically tolerated salts of the compounds of the formula I, especially acid addition salts with physiologically tolerated acids. Examples of suitable physiologically tolerated organic and inorganic acids are hydrochloric acid, hydrobromic acid, phosphoric acid, sulfuric acid, C_1-C_4-alkylsulfonic acids, such as methanesulfonic acid, aromatic sulfonic acids, such as benzenesulfonic acid and toluenesulfonic acid, oxalic acid, maleic acid, fumaric acid, lactic acid, tartaric acid, adipic acid and benzoic acid. Other utilizable acids are described in Fortschritte der Arzneimittelforschung [Advances in drug research], Volume 10, pages 224 ff., Birkhäuser Verlag, Basel and Stuttgart, 1966.

It is likewise possible to use N-oxides of the compounds of the formula I. In the N-oxides of the compounds of the formula I, one or more of the N atoms which is/are ring members, and in particular ring members in the aromatic heterocycles Q and/or Ar, are present as an N-oxide group. Preference is given to those N-oxides of the formula I in which the ring nitrogen atoms in the piperazine ring do not form any N-oxide group. Particularly preferred N-oxides exhibit a N-oxide group on one or two of the ring nitrogen atoms of Ar and/or Q.

Here and in that which follows, halogen is fluorine, chlorine, bromine or iodine.

C_n-C_m-Alkyl (in radicals such as alkoxy, alkylthio, alkylamino etc., as well) is a straight-chain or branched alkyl group having from n to m carbon atoms, e.g. from 1 to 4 carbon atoms. Examples of an alkyl group are methyl, ethyl, n-propyl, iso-propyl, n-butyl, 2-butyl, iso-butyl, tert-butyl, n-pentyl, 2-pentyl, neopentyl, n-hexyl and the like.

C_1-C_4-Haloalkyl is an alkyl group having from 1 to 4 C atoms in which all or some, e.g. 1, 2, 3 or 4 of the hydrogen atoms, is/are replaced by halogen atoms, in particular by chlorine or fluorine. Preferred haloalkyl is C_1-C_2-fluoroalkyl or C_1-C_2-fluorochloroalkyl, in particular CF_3, CHF_2, CF_2Cl, CH_2F, and CH_2CF_3.

C_1-C_4-Hydroxyalkyl is a C_1-C_4-alkyl group which possesses an OH group, such as 2-hydroxyethyl, 2-hydroxypropyl, 3-hydroxypropyl, 2-hydroxybutyl, 3-hydroxybutyl, 2-methyl-2-hydroxypropyl etc.

C_1-C_4-Alkoxy-C_1-C_4-alkyl is a C_1-C_4-alkyl group which carries a C_1-C_4-alkoxy substituent, e.g. methoxymethyl, ethoxymethyl, 2-methoxyethyl, 1-methoxyethyl, 2-ethoxyethyl, 1-ethoxyethyl, n-propoxymethyl, isopropoxymethyl, n-butoxymethyl, (1-methylpropoxy)methyl, (2-methylpropoxy)methyl, CH_2–$OC(CH_3)_3$, 2-(methoxy)ethyl, 2-(ethoxy)ethyl, 2-(n-propoxy)ethyl, 2-(1-methylethoxy)ethyl, 2-(n-butoxy)ethyl, 2-(1-methylpropoxy)ethyl, 2-(2-methylpropoxy)ethyl, 2-(1,1-dimethylethoxy)ethyl, 2-

(methoxy)propyl, 2-(ethoxy)propyl, 2-(n-propoxy)propyl, 2-(1-methylethoxy)propyl, 2-(n-butoxy)propyl, 2-(1-methylpropoxy)propyl, 2-(2-methylpropoxy)propyl, 2-(1,1-dimethylethoxy)propyl, 3-(methoxy)propyl, 3-(ethoxy)propyl, 3-(n-propoxy)propyl, 3-(1-methylethoxy)propyl, 3-(n-butoxy)propyl, 3-(1-methylpropoxy)propyl, 3-(2-methylpropoxy)propyl, 3-(1,1-dimethylethoxy)propyl, 2-(methoxy)butyl, 2-(ethoxy)butyl, 2-(n-propoxy)butyl, 2-(1-methylethoxy)butyl, 2-(n-butoxy)butyl, 2-(1-methylpropoxy)butyl, 2-(2-methylpropoxy)butyl, 2-(1,1-dimethylethoxy)butyl, 3-(methoxy)butyl, 3-(ethoxy)butyl, 3-(n-propoxy)butyl, 3-(1-methylethoxy)butyl, 3-(n-butoxy)butyl, 3-(1-methylpropoxy)butyl, 3-(2-methylpropoxy)butyl, 3-(1,1-dimethylethoxy)butyl, 4-(methoxy)butyl, 4-(ethoxy)butyl, 4-(n-propoxy)butyl, 4-(1-methylethoxy)butyl, 4-(n-butoxy)butyl, 4-(1-methylpropoxy)butyl, 4-(2-methylpropoxy)butyl or 4-(1,1-dimethylethoxy)butyl, preferably methoxymethyl, ethoxymethyl, 2-methoxyethyl, 2-ethoxyethyl, 2-(methoxy)propyl, 2-(ethoxy)propyl or 3-(methoxy)propyl, or 3-(ethoxy)propyl.

C_3-C_6-Cycloalkyl is a cycloaliphatic radical having from 3 to 6 C atoms, such as cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl.

C_3-C_6-Cycloalkyl-C_1-C_4-alkyl is a C_1-C_4-alkyl group which carries a C_3-C_6-cycloalkyl radical, e.g. cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, 1-cyclopropylethyl, 1-cyclobutylethyl, 1-cyclopentylethyl, 2-cyclopropylethyl, 2-cyclobutylethyl, 2-cyclopentylethyl, 1-cyclopropylpropyl, 1-cyclobutylpropyl, 1-cyclopentylpropyl, 2-cyclopropylpropyl, 2-cyclobutylpropyl, 2-cyclopentylpropyl, 3-cyclopropylpropyl, 3-cyclobutylpropyl, 3-cyclopentylpropyl, 1-cyclopropyl-1-methylethyl, 1-cyclopentyl-1-methylethyl, 1-cyclopentyl-1-methylethyl, 3-cyclohexylpropyl, 1-cyclohexyl-1-methylethyl, 1-cyclohexyl-1-methylethyl or 1-cyclohexyl-1-methylethyl.

C_2-C_4-Alkenyl is a singly unsaturated hydrocarbon radical having 2, 3, 4, 5 or 6 C-atoms, e.g. vinyl, allyl(2-propen-1-yl), 1-propen-1-yl, 2-propen-2-yl, methallyl(2-methylprop-2-en-1-yl) and the like. C_3-C_4-Alkenyl is, in particular, allyl, 1-methylprop-2-en-1-yl, 2-buten-1-yl, 3-buten-1-yl, methallyl, 2-penten-1-yl, 3-penten-1-yl, 4-penten-1-yl, 1-methylbut-2-en-1-yl or 2-ethylprop-2-en-1-yl.

C_3-C_6-Alkynyl is a hydrocarbon radical having 2, 3, 4, 5 or 6 C atoms which possesses a triple bond, e.g. propargyl (2-propyn-1-yl), 1-methylprop-2-yn-1-yl, 2-butyn-1-yl, 3-butyn-1-yl, 2-pentyn-1-yl, 1-pentyn-3-yl, etc.

Examples of 6-membered heteroaromatic radicals which possess 1 or 2 nitrogen atoms as ring members are, in particular, 2-, 3- or 4-pyridinyl, 2-, 4- or 5-pyrimidinyl, 2- or 3-pyrazinyl and 3- or 4-pyridazinyl. Examples of bivalent, 6-membered heteroaromatic

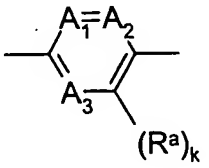
radicals which possess 1 or 2 nitrogen atoms as ring members are, in particular, pyridin-2,4-diyl, pyridin-2,5-diyl, pyridin-2,6-diyl, pyridin-3,5-diyl, pyrimidin-2,4-diyl, pyrimidin-2,5-diyl, pyrimidin-4,6-diyl, pyrazin-2,5-diyl, pyrazin-2,6-diyl, pyridazin-3,6-diyl and pyridazin-3,5-diyl.

With regard to using the compounds according to the invention as dopamine D_3 receptor ligands, preference is given to those compounds of formula I in which the piperazin ring is bonded to the heteroaromatic radical Q in the meta position or, in particular, in the para position with respect to the group $N(R^3)$-SO_2-Ar.

The heteroaromatic radical Q may be unsubstituted or possess a substituent R^a which is selected from halogen, C_1-C_4-alkyl and C_1-C_4-haloalkyl, in particular from chlorine, methyl and trifluoromethyl. In a preferred embodiment, Q is unsubstituted.

Preference is given to the variables Q, R^1, R^2, R^3 and Ar preferably having, independently of each other, the meanings given below:

Q is preferably a radical of the formula:



in which A_1, A_2 and A_3 are, independently of each other, N or CH, and one or two of the variables A_1, A_2 and A_3 can also be C-R^a, with A_1, A_2 and A_3 not simultaneously being N or being simultaneously selected from CH and C-R^a. In the formula, k is 0 or 1 and R^a has the previously mentioned meanings. In particular, R^a is selected from halogen, especially chlorine or fluorine, C_1-C_4-alkyl, especially methyl, and C_1-C_4-haloalkyl, especially trifluoromethyl. The C atom which is located between the atoms A_1 and A_3 preferably carries the piperazinyl radical. In particular, k = 0. In particular, none of the variables A^1, A^2 and A^3 is C-R^a. Preferred radicals Q are those in which A_1 and/or A_3 is/are N, the remaining variable A_1 or A_2 is CH or C-R^a, A_2 is CH, and the piperazinyl radical is bonded to the C atom which is located between A_1 and A_3. Among these, preference is furthermore given to compound I in which A_1 and A_2 are N and A_3 is CH or C-R^a.

In particular, Q is pyridin-2,5-diyl or pyrimidin-2,5-diyl which are unsubstituted or able to possess a substituent R^a which is different from hydrogen. The piperazinyl radical is then preferably arranged in the 2 position.

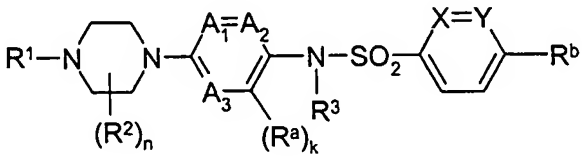
Ar is preferably phenyl or pyridyl which, where appropriate, possesses one or two of the abovementioned substituents R^b. With regard to using the compounds according to the invention as dopamine D_3 receptor ligands, preference is given to those compounds of formula I in which Ar carries one substituent R^b in the para position and, where appropriate, a further substituent R^b in the ortho position or metaposition, in each case related to the binding site for the sulfonamide group. The radicals R^b may be identical or different. Preference is given to the radicals R^b in the para position being selected from C_2-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_6-cycloalkyl and, in particular, from branched C_3-C_6-alkyl, especially isopropyl or C_3-C_6-cycloalkyl, especially cyclopropyl. Very particular preference is given to the radical R^b which is arranged in the para position of Ar being isopropyl. Preferred radicals R^b in the meta position or ortho position are selected from halogen, especially chlorine and fluorine, C_1-C_4-alkyl, especially methyl, CN, trifluoromethyl and difluoromethyl.

With regard to using the compounds according to the invention as dopamine D_3 receptor ligands, preference is given to those compounds of the formula I in which R^1 is different from hydrogen, in particular hydrogen and methyl. In particular, R^1 is C_2-C_3-alkyl, cyclopropylmethyl or, particularly preferably, ethyl, allyl or n-propyl.

The variable n is preferably 0 or 1. Provided n is $\neq 0$, R^2 is preferably methyl. When n is $\neq 0$, the group R^2 is preferably bonded to a carbon atom in the piperazine ring which is adjacent to the group R^1-N. In particularly preferred compounds, n = 0. Particular preference is also given to compounds of the formula I in which it applies that n = 1 and R^2 is a methyl group which is bonded to a carbon atom in the piperazine ring which is adjacent to the group R^1-N. The compounds can then be present as a racemate, as pure enantiomers or as nonracemic mixtures of the enantiomers. Among these, particular preference is given to those compounds in which the C atom which carries the methyl group exhibits the S configuration.

R^3 is preferably hydrogen or C_1-C_4-alkyl and, in particular, hydrogen.

Among the compounds of the general formula I, preference is given to the compounds of the general formula Ia

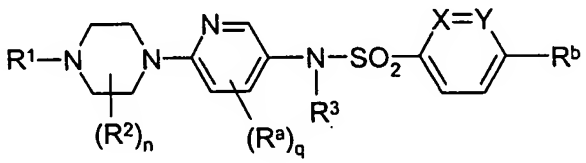


(Ia)

in which

n, R^1, R^2, R^3, R^a and R^b have the previously mentioned meanings, in particular the meanings specified as being preferred, and in which A_1, A_2 and A_3 are, independently of each other, N or CH, and one of the variables A_1, A_2 and A_3 can also be C-R^a, with A_1, A_2 and A_3 not simultaneously being N or simultaneously being selected from CH and C-R^a, and X and Y are selected from CH, C-$R^{b'}$ and N, in which $R^{b'}$ is halogen, methyl, CN, difluoromethyl or trifluoromethyl, with X and Y not simultaneously being N or simultaneously being C-$R^{b'}$, and k is 0 or 1. R^a has the previously mentioned meanings. In particular, R^a is selected from halogen, especially chlorine or fluorine, C_1-C_4-alkyl, especially methyl, and C_1-C_4-haloalkyl, especially trifluoromethyl. The C atom which is located between the atoms A_1 and A_3 preferably carries the piperazinyl radical. In particular, k = 0. In particular, none of the variables A^1, A^2 and A^3 is C-R^a. Preferred radicals Q are those in which A_1 and/or A_3 is/are N, the remaining variable A_1 or A_2 is CH or C-R^a, A_2 is CH, and the piperazinyl radical is bonded to the C atom which is located between A_1 and A_3. Among these, preference is furthermore given to compound I in which A_1 and A_2 are N and A_3 is CH or C-R^a. Among these, preference is given to those compounds of the formula Ia in which X or Y is CH or N and, in particular, both are CH.

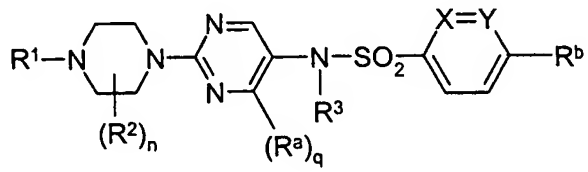
Among the compounds of general formula Ia, preference is given to the compounds of general formula Ia.1



(Ia.1)

in which n, X, Y, R^1, R^2, R^3, R^a and R^b have the previously mentioned meanings, in particular the meanings specified as being preferred, and q is 0, 1 or 2 and in particular 0.

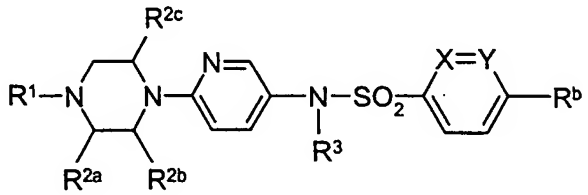
Among the compounds of general formula Ia, preference is furthermore given to the compounds of general formula Ia.2



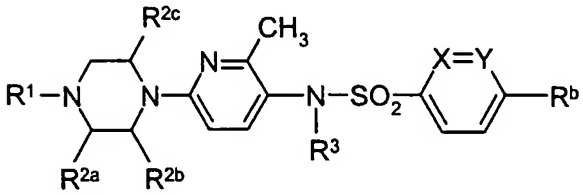
(Ia.2)

in which n, X, Y, R^1, R^2, R^3, R^a and R^b have the previously mentioned meanings, in particular the meanings specified as being preferred, and q is 0, 1 or 2 and, in particular, 0.

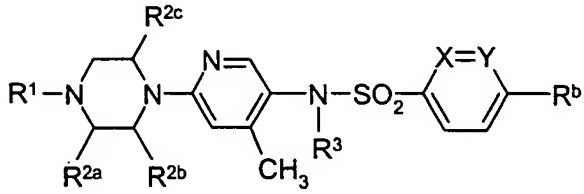
Examples of compounds of the formula Ia.1 are the compounds of the following general formulae Ia.1a, Ia.1b, Ia.1c, Ia.1d, Ia.1e, Ia.1f and Ia.1g:



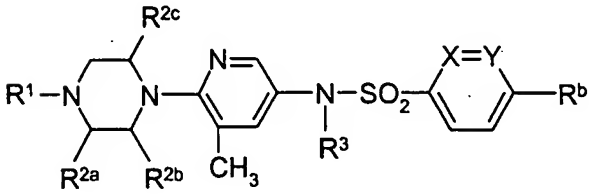
(Ia.1a)



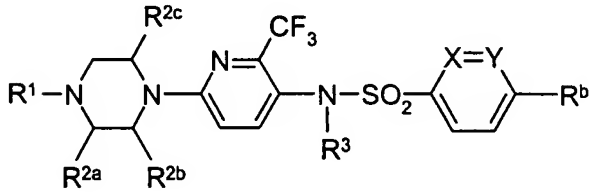
(Ia.1b)



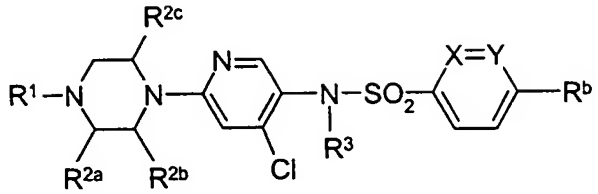
(Ia.1c)



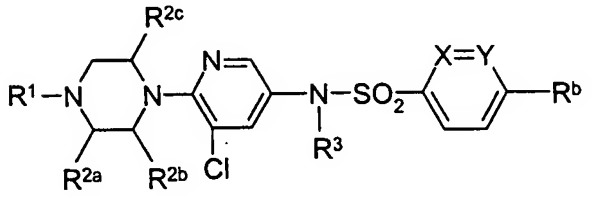
(Ia.1d)



(Ia.1e)



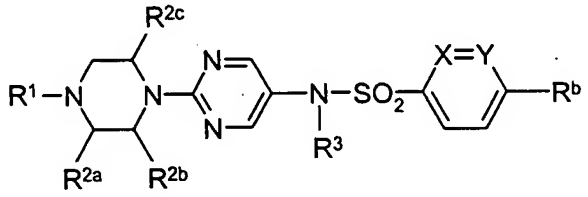
(Ia.1f)



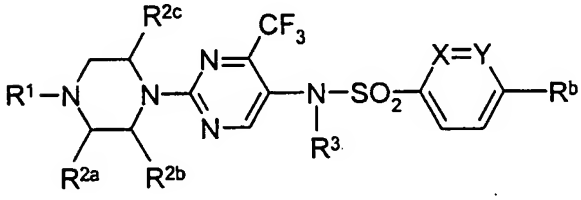
(Ia.1g)

in which R^1, R^{2a}, R^{2b}, R^{2c}, R^3, X, Y and R^b, have the meanings specified in one line in Table 1.

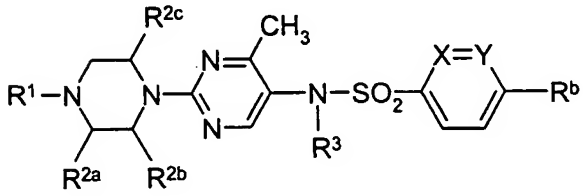
Examples of compounds of the formula Ia.2 are the compounds of the following general formulae Ia.2a, Ia.2b and Ia.2c:



(Ia.2a)



(Ia.2b)



(Ia.2c)

in which R^1, R^{2a}, R^{2b}, R^{2c}, R^3, X, Y and R^b have the meanings specified in one line in Table 1.

Table 1:

M/44060

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
1.	H	H	H	H	H	CH	CH	$CH(CH_3)_2$
2.	CH_3	H	H	H	H	CH	CH	$CH(CH_3)_2$
3.	CH_2CH_3	H	H	H	H	CH	CH	$CH(CH_3)_2$
4.	$CH_2CH=CH_2$	H	H	H	H	CH	CH	$CH(CH_3)_2$
5.	CH_2-c-C_3H_5	H	H	H	H	CH	CH	$CH(CH_3)_2$
6.	$CH_2CH_2CH_3$	H	H	H	H	CH	CH	$CH(CH_3)_2$
7.	H	(s)CH_3	H	H	H	CH	CH	$CH(CH_3)_2$
8.	CH_3	(s)CH_3	H	H	H	CH	CH	$CH(CH_3)_2$
9.	CH_2CH_3	(s)CH_3	H	H	H	CH	CH	$CH(CH_3)_2$
10.	$CH_2CH=CH_2$	(s)CH_3	H	H	H	CH	CH	$CH(CH_3)_2$
11.	CH_2-c-C_3H_5	(s)CH_3	H	H	H	CH	CH	$CH(CH_3)_2$
12.	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	CH	CH	$CH(CH_3)_2$
13.	CH_3	*rac*- CH_3	H	H	H	CH	CH	$CH(CH_3)_2$
14.	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	CH	CH	$CH(CH_3)_2$
15.	CH_2-c-C_3H_5	*rac*- CH_3	H	H	H	CH	CH	$CH(CH_3)_2$
16.	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	CH	CH	$CH(CH_3)_2$
17.	CH_3	(R)CH_3	H	H	H	CH	CH	$CH(CH_3)_2$
18.	$CH_2CH=CH_2$	(R)CH_3	H	H	H	CH	CH	$CH(CH_3)_2$
19.	CH_2-c-C_3H_5	(R)CH_3	H	H	H	CH	CH	$CH(CH_3)_2$
20.	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	CH	CH	$CH(CH_3)_2$
21.	CH_3	H	CH_3	H	H	CH	CH	$CH(CH_3)_2$
22.	$CH_2CH=CH_2$	H	CH_3	H	H	CH	CH	$CH(CH_3)_2$
23.	CH_2-c-C_3H_5	H	CH_3	H	H	CH	CH	$CH(CH_3)_2$
24.	$CH_2CH_2CH_3$	H	CH_3	H	H	CH	CH	$CH(CH_3)_2$
25.	CH_3	CH_3	H	CH_3	H	CH	CH	$CH(CH_3)_2$
26.	$CH_2CH=CH_2$	CH_3	H	CH_3	H	CH	CH	$CH(CH_3)_2$
27.	CH_2-c-C_3H_5	CH_3	H	CH_3	H	CH	CH	$CH(CH_3)_2$
28.	$CH_2CH_2CH_3$	CH_3	H	CH_3	H	CH	CH	$CH(CH_3)_2$
29.	CH_3	CH_3	CH_3	H	H	CH	CH	$CH(CH_3)_2$
30.	$CH_2CH=CH_2$	CH_3	CH_3	H	H	CH	CH	$CH(CH_3)_2$
31.	CH_2-c-C_3H_5	CH_3	CH_3	H	H	CH	CH	$CH(CH_3)_2$
32.	$CH_2CH_2CH_3$	CH_3	CH_3	H	H	CH	CH	$CH(CH_3)_2$
33.	(s)$(CH_2)_3$		H	H	H	CH	CH	$CH(CH_3)_2$
34.	(s)$(CH_2)_4$		H	H	H	CH	CH	$CH(CH_3)_2$
35.	*rac*$(CH_2)_3$		H	H	H	CH	CH	$CH(CH_3)_2$
36.	*rac* $(CH_2)_4$		H	H	H	CH	CH	$CH(CH_3)_2$
37.	(R)$(CH_2)_3$		H	H	H	CH	CH	$CH(CH_3)_2$
38.	(R)$(CH_2)_4$		H	H	H	CH	CH	$CH(CH_3)_2$
39.	H	H	H	H	CH_3	CH	CH	$CH(CH_3)_2$
40.	CH_3	H	H	H	CH_3	CH	CH	$CH(CH_3)_2$

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
41.	CH_2CH_3	H	H	H	CH_3	CH	CH	$CH(CH_3)_2$
42.	$CH_2CH=CH_2$	H	H	H	CH_3	CH	CH	$CH(CH_3)_2$
43.	CH_2-c-C_3H_5	H	H	H	CH_3	CH	CH	$CH(CH_3)_2$
44.	$CH_2CH_2CH_3$	H	H	H	CH_3	CH	CH	$CH(CH_3)_2$
45.	H	(s)CH_3	H	H	CH_3	CH	CH	$CH(CH_3)_2$
46.	CH_3	(s)CH_3	H	H	CH_3	CH	CH	$CH(CH_3)_2$
47.	CH_2CH_3	(s)CH_3	H	H	CH_3	CH	CH	$CH(CH_3)_2$
48.	$CH_2CH=CH_2$	(s)CH_3	H	H	CH_3	CH	CH	$CH(CH_3)_2$
49.	CH_2-c-C_3H_5	(s)CH_3	H	H	CH_3	CH	CH	$CH(CH_3)_2$
50.	$CH_2CH_2CH_3$	(s)CH_3	H	H	CH_3	CH	CH	$CH(CH_3)_2$
51.	CH_3	*rac*- CH_3	H	H	CH_3	CH	CH	$CH(CH_3)_2$
52.	$CH_2CH=CH_2$	*rac*- CH_3	H	H	CH_3	CH	CH	$CH(CH_3)_2$
53.	CH_2-c-C_3H_5	*rac*- CH_3	H	H	CH_3	CH	CH	$CH(CH_3)_2$
54.	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	CH_3	CH	CH	$CH(CH_3)_2$
55.	CH_3	(R)CH_3	H	H	CH_3	CH	CH	$CH(CH_3)_2$
56.	$CH_2CH=CH_2$	(R)CH_3	H	H	CH_3	CH	CH	$CH(CH_3)_2$
57.	CH_2-c-C_3H_5	(R)CH_3	H	H	CH_3	CH	CH	$CH(CH_3)_2$
58.	$CH_2CH_2CH_3$	(R)CH_3	H	H	CH_3	CH	CH	$CH(CH_3)_2$
59.	CH_3	H	CH_3	H	CH_3	CH	CH	$CH(CH_3)_2$
60.	$CH_2CH=CH_2$	H	CH_3	H	CH_3	CH	CH	$CH(CH_3)_2$
61.	CH_2-c-C_3H_5	H	CH_3	H	CH_3	CH	CH	$CH(CH_3)_2$
62.	$CH_2CH_2CH_3$	H	CH_3	H	CH_3	CH	CH	$CH(CH_3)_2$
63.	CH_3	CH_3	H	CH_3	CH_3	CH	CH	$CH(CH_3)_2$
64.	$CH_2CH=CH_2$	CH_3	H	CH_3	CH_3	CH	CH	$CH(CH_3)_2$
65.	CH_2-c-C_3H_5	CH_3	H	CH_3	CH_3	CH	CH	$CH(CH_3)_2$
66.	$CH_2CH_2CH_3$	CH_3	H	CH_3	CH_3	CH	CH	$CH(CH_3)_2$
67.	CH_3	CH_3	CH_3	H	CH_3	CH	CH	$CH(CH_3)_2$
68.	$CH_2CH=CH_2$	CH_3	CH_3	H	CH_3	CH	CH	$CH(CH_3)_2$
69.	CH_2-c-C_3H_5	CH_3	CH_3	H	CH_3	CH	CH	$CH(CH_3)_2$
70.	$CH_2CH_2CH_3$	CH_3	CH_3	H	CH_3	CH	CH	$CH(CH_3)_2$
71.	(S)$(CH_2)_3$		H	H	CH_3	CH	CH	$CH(CH_3)_2$
72.	(S)$(CH_2)_4$		H	H	CH_3	CH	CH	$CH(CH_3)_2$
73.	*rac*$(CH_2)_3$		H	H	CH_3	CH	CH	$CH(CH_3)_2$
74.	*rac*$(CH_2)_4$		H	H	CH_3	CH	CH	$CH(CH_3)_2$
75.	(R)$(CH_2)_3$		H	H	CH_3	CH	CH	$CH(CH_3)_2$
76.	(R)$(CH_2)_4$		H	H	CH_3	CH	CH	$CH(CH_3)_2$
77.	$CH_2CH=CH_2$	H	H	H	H	C-Cl	CH	$CH(CH_3)_2$
78.	CH_2-c-C_3H_5	H	H	H	H	C-Cl	CH	$CH(CH_3)_2$
79.	$CH_2CH_2CH_3$	H	H	H	H	C-Cl	CH	$CH(CH_3)_2$
80.	$CH_2CH=CH_2$	(s)CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
81.	CH_2-c-C_3H_5	(s)CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
82.	CH_2CH_3	(s)CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
83.	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
84.	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
85.	CH_2-c-C_3H_5	*rac*- CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
86.	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
87.	CH_2CH_3	*rac*- CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
88.	$CH_2CH=CH_2$	(R)CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
89.	CH_2-c-C_3H_5	(R)CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
90.	CH_2CH_3	(R)CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
91.	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	C-Cl	CH	$CH(CH_3)_2$
92.	$CH_2CH=CH_2$	H	CH_3	H	H	C-Cl	CH	$CH(CH_3)_2$
93.	CH_2-c-C_3H_5	H	CH_3	H	H	C-Cl	CH	$CH(CH_3)_2$
94.	$CH_2CH_2CH_3$	H	CH_3	H	H	C-Cl	CH	$CH(CH_3)_2$
95.	$CH_2CH=CH_2$	CH_3	H	CH_3	H	C-Cl	CH	$CH(CH_3)_2$
96.	CH_2-c-C_3H_5	CH_3	H	CH_3	H	C-Cl	CH	$CH(CH_3)_2$
97.	$CH_2CH_2CH_3$	CH_3	H	CH_3	H	C-Cl	CH	$CH(CH_3)_2$
98.	$CH_2CH=CH_2$	CH_3	CH_3	H	H	C-Cl	CH	$CH(CH_3)_2$
99.	CH_2-c-C_3H_5	CH_3	CH_3	H	H	C-Cl	CH	$CH(CH_3)_2$
100	$CH_2CH_2CH_3$	CH_3	CH_3	H	H	C-Cl	CH	$CH(CH_3)_2$
101	$(CH_2)_3$		H	H	H	C-Cl	CH	$CH(CH_3)_2$
102	$(CH_2)_4$		H	H	H	C-Cl	CH	$CH(CH_3)_2$
103	$CH_2CH=CH_2$	H	H	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
104	CH_2-c-C_3H_5	H	H	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
105	$CH_2CH_2CH_3$	H	H	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
106	$CH_2CH=CH_2$	(s)CH_3	H	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
107	CH_2-c-C_3H_5	(s)CH_3	H	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
108	CH_2CH_3	(s)CH_3	H	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
109	$CH_2CH_2CH_3$	(s)CH_3	H	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
110	$CH_2CH=CH_2$	*rac*- CH_3	H	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
111	CH_2-c-C_3H_5	*rac*- CH_3	H	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
112	CH_2CH_3	*rac*- CH_3	H	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
113	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
114	$CH_2CH=CH_2$	(R)CH_3	H	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
115	CH_2-c-C_3H_5	(R)CH_3	H	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
116	$CH_2CH_2CH_3$	(R)CH_3	H	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
117	CH_2CH_3	(R)CH_3	H	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
118	$CH_2CH=CH_2$	H	CH_3	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
119	CH_2-c-C_3H_5	H	CH_3	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
120	$CH_2CH_2CH_3$	H	CH_3	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
121	$CH_2CH=CH_2$	CH_3	H	CH_3	CH_3	C-Cl	CH	$CH(CH_3)_2$
122	CH_2-c-C_3H_5	CH_3	H	CH_3	CH_3	C-Cl	CH	$CH(CH_3)_2$
123	$CH_2CH_2CH_3$	CH_3	H	CH_3	CH_3	C-Cl	CH	$CH(CH_3)_2$
124	$CH_2CH=CH_2$	CH_3	CH_3	H	CH_3	C-Cl	CH	$CH(CH_3)_2$

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
125	CH_2-c-C_3H_5	CH_3	CH_3	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
126	$CH_2CH_2CH_3$	CH_3	CH_3	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
127	$(CH_2)_3$		H	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
128	$(CH_2)_4$		H	H	CH_3	C-Cl	CH	$CH(CH_3)_2$
129	$CH_2CH=CH_2$	H	H	H	H	CH	C-Cl	$CH(CH_3)_2$
130	CH_2-c-C_3H_5	H	H	H	H	CH	C-Cl	$CH(CH_3)_2$
131	$CH_2CH_2CH_3$	H	H	H	H	CH	C-Cl	$CH(CH_3)_2$
132	$CH_2CH=CH_2$	(s)CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
133	CH_2-c-C_3H_5	(s)CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
134	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
135	CH_2CH_3	(s)CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
136	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
137	CH_2-c-C_3H_5	*rac*- CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
138	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
139	CH_2CH_3	*rac*- CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
140	$CH_2CH=CH_2$	(R)CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
141	CH_2-c-C_3H_5	(R)CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
142	CH_2CH_3	(R)CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
143	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	CH	C-Cl	$CH(CH_3)_2$
144	$CH_2CH=CH_2$	H	CH_3	H	H	CH	C-Cl	$CH(CH_3)_2$
145	CH_2-c-C_3H_5	H	CH_3	H	H	CH	C-Cl	$CH(CH_3)_2$
146	$CH_2CH_2CH_3$	H	CH_3	H	H	CH	C-Cl	$CH(CH_3)_2$
147	$CH_2CH=CH_2$	CH_3	H	CH_3	H	CH	C-Cl	$CH(CH_3)_2$
148	CH_2-c-C_3H_5	CH_3	H	CH_3	H	CH	C-Cl	$CH(CH_3)_2$
149	$CH_2CH_2CH_3$	CH_3	H	CH_3	H	CH	C-Cl	$CH(CH_3)_2$
150	$CH_2CH=CH_2$	CH_3	CH_3	H	H	CH	C-Cl	$CH(CH_3)_2$
151	CH_2-c-C_3H_5	CH_3	CH_3	H	H	CH	C-Cl	$CH(CH_3)_2$
152	$CH_2CH_2CH_3$	CH_3	CH_3	H	H	CH	C-Cl	$CH(CH_3)_2$
153	$(CH_2)_3$		H	H	H	CH	C-Cl	$CH(CH_3)_2$
154	$(CH_2)_4$		H	H	H	CH	C-Cl	$CH(CH_3)_2$
155	$CH_2CH=CH_2$	H	H	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
156	CH_2-c-C_3H_5	H	H	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
157	$CH_2CH_2CH_3$	H	H	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
158	$CH_2CH=CH_2$	(s)CH_3	H	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
159	CH_2-c-C_3H_5	(s)CH_3	H	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
160	$CH_2CH_2CH_3$	(s)CH_3	H	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
161	CH_2CH_3	(s)CH_3	H	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
162	$CH_2CH=CH_2$	*rac*- CH_3	H	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
163	CH_2-c-C_3H_5	*rac*- CH_3	H	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
164	CH_2CH_3	*rac*- CH_3	H	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
165	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
166	$CH_2CH=CH_2$	(R)CH_3	H	H	CH_3	CH	C-Cl	$CH(CH_3)_2$

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
167	CH_2-c-C_3H_5	(R)CH_3	H	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
168	CH_2CH_3	(R)CH_3	H	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
169	$CH_2CH_2CH_3$	(R)CH_3	H	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
170	$CH_2CH=CH_2$	H	CH_3	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
171	CH_2-c-C_3H_5	H	CH_3	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
172	$CH_2CH_2CH_3$	H	CH_3	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
173	$CH_2CH=CH_2$	CH_3	H	CH_3	CH_3	CH	C-Cl	$CH(CH_3)_2$
174	CH_2-c-C_3H_5	CH_3	H	CH_3	CH_3	CH	C-Cl	$CH(CH_3)_2$
175	$CH_2CH_2CH_3$	CH_3	H	CH_3	CH_3	CH	C-Cl	$CH(CH_3)_2$
176	$CH_2CH=CH_2$	CH_3	CH_3	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
177	CH_2-c-C_3H_5	CH_3	CH_3	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
178	$CH_2CH_2CH_3$	CH_3	CH_3	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
179	$(CH_2)_3$		H	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
180	$(CH_2)_4$		H	H	CH_3	CH	C-Cl	$CH(CH_3)_2$
181	$CH_2CH=CH_2$	H	H	H	H	C-CH_3	CH	$CH(CH_3)_2$
182	CH_2-c-C_3H_5	H	H	H	H	C-CH_3	CH	$CH(CH_3)_2$
183	$CH_2CH_2CH_3$	H	H	H	H	C-CH_3	CH	$CH(CH_3)_2$
184	$CH_2CH=CH_2$	(s)CH_3	H	H	H	C-CH_3	CH	$CH(CH_3)_2$
185	CH_2-c-C_3H_5	(s)CH_3	H	H	H	C-CH_3	CH	$CH(CH_3)_2$
186	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	C-CH_3	CH	$CH(CH_3)_2$
187	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	C-CH_3	CH	$CH(CH_3)_2$
188	CH_2-c-C_3H_5	*rac*- CH_3	H	H	H	C-CH_3	CH	$CH(CH_3)_2$
189	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	C-CH_3	CH	$CH(CH_3)_2$
190	$CH_2CH=CH_2$	(R)CH_3	H	H	H	C-CH_3	CH	$CH(CH_3)_2$
191	CH_2-c-C_3H_5	(R)CH_3	H	H	H	C-CH_3	CH	$CH(CH_3)_2$
192	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	C-CH_3	CH	$CH(CH_3)_2$
193	$CH_2CH=CH_2$	H	CH_3	H	H	C-CH_3	CH	$CH(CH_3)_2$
194	CH_2-c-C_3H_5	H	CH_3	H	H	C-CH_3	CH	$CH(CH_3)_2$
195	$CH_2CH_2CH_3$	H	CH_3	H	H	C-CH_3	CH	$CH(CH_3)_2$
196	$CH_2CH=CH_2$	CH_3	H	CH_3	H	C-CH_3	CH	$CH(CH_3)_2$
197	CH_2-c-C_3H_5	CH_3	H	CH_3	H	C-CH_3	CH	$CH(CH_3)_2$
198	$CH_2CH_2CH_3$	CH_3	H	CH_3	H	C-CH_3	CH	$CH(CH_3)_2$
199	$CH_2CH=CH_2$	CH_3	CH_3	H	H	C-CH_3	CH	$CH(CH_3)_2$
200	CH_2-c-C_3H_5	CH_3	CH_3	H	H	C-CH_3	CH	$CH(CH_3)_2$
201	$CH_2CH_2CH_3$	CH_3	CH_3	H	H	C-CH_3	CH	$CH(CH_3)_2$
202	$(CH_2)_3$		H	H	H	C-CH_3	CH	$CH(CH_3)_2$
203	$(CH_2)_4$		H	H	H	C-CH_3	CH	$CH(CH_3)_2$
204	$CH_2CH=CH_2$	H	H	H	CH_3	C-CH_3	CH	$CH(CH_3)_2$
205	CH_2-c-C_3H_5	H	H	H	CH_3	C-CH_3	CH	$CH(CH_3)_2$
206	$CH_2CH_2CH_3$	H	H	H	CH_3	C-CH_3	CH	$CH(CH_3)_2$
207	$CH_2CH=CH_2$	(s)CH_3	H	H	CH_3	C-CH_3	CH	$CH(CH_3)_2$
208	CH_2-c-C_3H_5	(s)CH_3	H	H	CH_3	C-CH_3	CH	$CH(CH_3)_2$

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
209	$CH_2CH_2CH_3$	(s)CH_3	H	H	CH_3	C-CH_3	CH	$CH(CH_3)_2$
210	$CH_2CH=CH_2$	*rac*- CH_3	H	H	CH_3	C-CH_3	CH	$CH(CH_3)_2$
211	CH_2-c-C_3H_5	*rac*- CH_3	H	H	CH_3	C-CH_3	CH	$CH(CH_3)_2$
212	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	CH_3	C-CH_3	CH	$CH(CH_3)_2$
213	$CH_2CH=CH_2$	(R)CH_3	H	H	CH_3	C-CH_3	CH	$CH(CH_3)_2$
214	CH_2-c-C_3H_5	(R)CH_3	H	H	CH_3	C-CH_3	CH	$CH(CH_3)_2$
215	$CH_2CH_2CH_3$	(R)CH_3	H	H	CH_3	C-CH_3	CH	$CH(CH_3)_2$
216	$CH_2CH=CH_2$	H	CH_3	H	CH_3	C-CH_3	CH	$CH(CH_3)_2$
217	CH_2-c-C_3H_5	H	CH_3	H	CH_3	C-CH_3	CH	$CH(CH_3)_2$
218	$CH_2CH_2CH_3$	H	CH_3	H	CH_3	C-CH_3	CH	$CH(CH_3)_2$
219	$CH_2CH=CH_2$	CH_3	H	CH_3	CH_3	C-CH_3	CH	$CH(CH_3)_2$
220	CH_2-c-C_3H_5	CH_3	H	CH_3	CH_3	C-CH_3	CH	$CH(CH_3)_2$
221	$CH_2CH_2CH_3$	CH_3	H	CH_3	CH_3	C-CH_3	CH	$CH(CH_3)_2$
222	$CH_2CH=CH_2$	CH_3	CH_3	H	CH_3	C-CH_3	CH	$CH(CH_3)_2$
223	CH_2-c-C_3H_5	CH_3	CH_3	H	CH_3	C-CH_3	CH	$CH(CH_3)_2$
224	$CH_2CH_2CH_3$	CH_3	CH_3	H	CH_3	C-CH_3	CH	$CH(CH_3)_2$
225	$(CH_2)_3$		H	H	CH_3	C-CH_3	CH	$CH(CH_3)_2$
226	$(CH_2)_4$		H	H	CH_3	C-CH_3	CH	$CH(CH_3)_2$
227	$CH_2CH=CH_2$	H	H	H	H	CH	C-CH_3	$CH(CH_3)_2$
228	CH_2-c-C_3H_5	H	H	H	H	CH	C-CH_3	$CH(CH_3)_2$
229	$CH_2CH_2CH_3$	H	H	H	H	CH	C-CH_3	$CH(CH_3)_2$
230	$CH_2CH=CH_2$	(s)CH_3	H	H	H	CH	C-CH_3	$CH(CH_3)_2$
231	CH_2-c-C_3H_5	(s)CH_3	H	H	H	CH	C-CH_3	$CH(CH_3)_2$
232	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	CH	C-CH_3	$CH(CH_3)_2$
233	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	CH	C-CH_3	$CH(CH_3)_2$
234	CH_2-c-C_3H_5	*rac*- CH_3	H	H	H	CH	C-CH_3	$CH(CH_3)_2$
235	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	CH	C-CH_3	$CH(CH_3)_2$
236	$CH_2CH=CH_2$	(R)CH_3	H	H	H	CH	C-CH_3	$CH(CH_3)_2$
237	CH_2-c-C_3H_5	(R)CH_3	H	H	H	CH	C-CH_3	$CH(CH_3)_2$
238	$CH_2CH_2CH_3$	(T)CH_3	H	H	H	CH	C-CH_3	$CH(CH_3)_2$
239	$CH_2CH=CH_2$	H	CH_3	H	H	CH	C-CH_3	$CH(CH_3)_2$
240	CH_2-c-C_3H_5	H	CH_3	H	H	CH	C-CH_3	$CH(CH_3)_2$
241	$CH_2CH_2CH_3$	H	CH_3	H	H	CH	C-CH_3	$CH(CH_3)_2$
242	$CH_2CH=CH_2$	CH_3	H	CH_3	H	CH	C-CH_3	$CH(CH_3)_2$
243	CH_2-c-C_3H_5	CH_3	H	CH_3	H	CH	C-CH_3	$CH(CH_3)_2$
244	$CH_2CH_2CH_3$	CH_3	H	CH_3	H	CH	C-CH_3	$CH(CH_3)_2$
245	$CH_2CH=CH_2$	CH_3	CH_3	H	H	CH	C-CH_3	$CH(CH_3)_2$
246	CH_2-c-C_3H_5	CH_3	CH_3	H	H	CH	C-CH_3	$CH(CH_3)_2$
247	$CH_2CH_2CH_3$	CH_3	CH_3	H	H	CH	C-CH_3	$CH(CH_3)_2$
248	$(CH_2)_3$		H	H	H	CH	C-CH_3	$CH(CH_3)_2$
249	$(CH_2)_4$		H	H	H	CH	C-CH_3	$CH(CH_3)_2$
250	$CH_2CH=CH_2$	H	H	H	CH_3	CH	C-CH_3	$CH(CH_3)_2$

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
251	CH_2-c-C_3H_5	H	H	H	CH_3	CH	C-CH_3	$CH(CH_3)_2$
252	$CH_2CH_2CH_3$	H	H	H	CH_3	CH	C-CH_3	$CH(CH_3)_2$
253	$CH_2CH=CH_2$	(s)CH_3	H	H	CH_3	CH	C-CH_3	$CH(CH_3)_2$
254	CH_2-c-C_3H_5	(s)CH_3	H	H	CH_3	CH	C-CH_3	$CH(CH_3)_2$
255	$CH_2CH_2CH_3$	(s)CH_3	H	H	CH_3	CH	C-CH_3	$CH(CH_3)_2$
256	$CH_2CH=CH_2$	*rac*- CH_3	H	H	CH_3	CH	C-CH_3	$CH(CH_3)_2$
257	CH_2-c-C_3H_5	*rac*- CH_3	H	H	CH_3	CH	C-CH_3	$CH(CH_3)_2$
258	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	CH_3	CH	C-CH_3	$CH(CH_3)_2$
259	$CH_2CH=CH_2$	(R)CH_3	H	H	CH_3	CH	C-CH_3	$CH(CH_3)_2$
260	CH_2-c-C_3H_5	(R)CH_3	H	H	CH_3	CH	C-CH_3	$CH(CH_3)_2$
261	$CH_2CH_2CH_3$	(R)CH_3	H	H	CH_3	CH	C-CH_3	$CH(CH_3)_2$
262	$CH_2CH=CH_2$	H	CH_3	H	CH_3	CH	C-CH_3	$CH(CH_3)_2$
263	CH_2-c-C_3H_5	H	CH_3	H	CH_3	CH	C-CH_3	$CH(CH_3)_2$
264	$CH_2CH_2CH_3$	H	CH_3	H	CH_3	CH	C-CH_3	$CH(CH_3)_2$
265	$CH_2CH=CH_2$	CH_3	H	CH_3	CH_3	CH	C-CH_3	$CH(CH_3)_2$
266	CH_2-c-C_3H_5	CH_3	H	CH_3	CH_3	CH	C-CH_3	$CH(CH_3)_2$
267	$CH_2CH_2CH_3$	CH_3	H	CH_3	CH_3	CH	C-CH_3	$CH(CH_3)_2$
268	$CH_2CH=CH_2$	CH_3	CH_3	H	CH_3	CH	C-CH_3	$CH(CH_3)_2$
269	CH_2-c-C_3H_5	CH_3	CH_3	H	CH_3	CH	C-CH_3	$CH(CH_3)_2$
270	$CH_2CH_2CH_3$	CH_3	CH_3	H	CH_3	CH	C-CH_3	$CH(CH_3)_2$
271	$(CH_2)_3$		H	H	CH_3	CH	C-CH_3	$CH(CH_3)_2$
272	$(CH_2)_4$		H	H	CH_3	CH	C-CH_3	$CH(CH_3)_2$
273	H	H	H	H	H	CH	CH	c-C_3H_5
274	CH_3	H	H	H	H	CH	CH	c-C_3H_5
275	CH_2CH_3	H	H	H	H	CH	CH	c-C_3H_5
276	$CH_2CH=CH_2$	H	H	H	H	CH	CH	c-C_3H_5
277	CH_2-c-C_3H_5	H	H	H	H	CH	CH	c-C_3H_5
278	$CH_2CH_2CH_3$	H	H	H	H	CH	CH	c-C_3H_5
279	H	(s)CH_3	H	H	H	CH	CH	c-C_3H_5
280	CH_3	(s)CH_3	H	H	H	CH	CH	c-C_3H_5
281	CH_2CH_3	(s)CH_3	H	H	H	CH	CH	c-C_3H_5
282	$CH_2CH=CH_2$	(s)CH_3	H	H	H	CH	CH	c-C_3H_5
283	CH_2-c-C_3H_5	(s)CH_3	H	H	H	CH	CH	c-C_3H_5
284	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	CH	CH	c-C_3H_5
285	CH_3	*rac*- CH_3	H	H	H	CH	CH	c-C_3H_5
286	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	CH	CH	c-C_3H_5
287	CH_2-c-C_3H_5	*rac*- CH_3	H	H	H	CH	CH	c-C_3H_5
288	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	CH	CH	c-C_3H_5
289	CH_2CH_3	(R)CH_3	H	H	H	CH	CH	c-C_3H_5
290	$CH_2CH=CH_2$	(R)CH_3	H	H	H	CH	CH	c-C_3H_5
291	CH_2-c-C_3H_5	(R)CH_3	H	H	H	CH	CH	c-C_3H_5
292	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	CH	CH	c-C_3H_5

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
293	CH_3	H	CH_3	H	H	CH	CH	c-C_3H_5
294	$CH_2CH=CH_2$	H	CH_3	H	H	CH	CH	c-C_3H_5
295	CH_2-c-C_3H_5	H	CH_3	H	H	CH	CH	c-C_3H_5
296	$CH_2CH_2CH_3$	H	CH_3	H	H	CH	CH	c-C_3H_5
297	CH_3	CH_3	H	CH_3	H	CH	CH	c-C_3H_5
298	$CH_2CH=CH_2$	CH_3	H	CH_3	H	CH	CH	c-C_3H_5
299	CH_2-c-C_3H_5	CH_3	H	CH_3	H	CH	CH	c-C_3H_5
300	$CH_2CH_2CH_3$	CH_3	H	CH_3	H	CH	CH	c-C_3H_5
301	CH_3	CH_3	CH_3	H	H	CH	CH	c-C_3H_5
302	$CH_2CH=CH_2$	CH_3	CH_3	H	H	CH	CH	c-C_3H_5
303	CH_2-c-C_3H_5	CH_3	CH_3	H	H	CH	CH	c-C_3H_5
304	$CH_2CH_2CH_3$	CH_3	CH_3	H	H	CH	CH	c-C_3H_5
305	(s)$(CH_2)_3$		H	H	H	CH	CH	c-C_3H_5
306	(s)$(CH_2)_4$		H	H	H	CH	CH	c-C_3H_5
307	*rac*$(CH_2)_3$		H	H	H	CH	CH	c-C_3H_5
308	*rac*$(CH_2)_4$		H	H	H	CH	CH	c-C_3H_5
309	(R)$(CH_2)_3$		H	H	H	CH	CH	c-C_3H_5
310	(R)$(CH_2)_4$		H	H	H	CH	CH	c-C_3H_5
311	H	H	H	H	CH_3	CH	CH	c-C_3H_5
312	CH_3	H	H	H	CH_3	CH	CH	c-C_3H_5
313	CH_2CH_3	H	H	H	CH_3	CH	CH	c-C_3H_5
314	$CH_2CH=CH_2$	H	H	H	CH_3	CH	CH	c-C_3H_5
315	CH_2-c-C_3H_5	H	H	H	CH_3	CH	CH	c-C_3H_5
316	$CH_2CH_2CH_3$	H	H	H	CH_3	CH	CH	c-C_3H_5
317	H	(s)CH_3	H	H	CH_3	CH	CH	c-C_3H_5
318	CH_3	(s)CH_3	H	H	CH_3	CH	CH	c-C_3H_5
319	CH_2CH_3	(s)CH_3	H	H	CH_3	CH	CH	c-C_3H_5
320	$CH_2CH=CH_2$	(s)CH_3	H	H	CH_3	CH	CH	c-C_3H_5
321	CH_2-c-C_3H_5	(s)CH_3	H	H	CH_3	CH	CH	c-C_3H_5
322	$CH_2CH_2CH_3$	(s)CH_3	H	H	CH_3	CH	CH	c-C_3H_5
323	CH_3	*rac*- CH_3	H	H	CH_3	CH	CH	c-C_3H_5
324	$CH_2CH=CH_2$	*rac*- CH_3	H	H	CH_3	CH	CH	c-C_3H_5
325	CH_2-c-C_3H_5	*rac*- CH_3	H	H	CH_3	CH	CH	c-C_3H_5
326	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	CH_3	CH	CH	c-C_3H_5
327	CH_2CH_3	(R)CH_3	H	H	CH_3	CH	CH	c-C_3H_5
328	$CH_2CH=CH_2$	(R)CH_3	H	H	CH_3	CH	CH	c-C_3H_5
329	CH_2-c-C_3H_5	(R)CH_3	H	H	CH_3	CH	CH	c-C_3H_5
330	$CH_2CH_2CH_3$	(R)CH_3	H	H	CH_3	CH	CH	c-C_3H_5
331	CH_3	H	CH_3	H	CH_3	CH	CH	c-C_3H_5
332	$CH_2CH=CH_2$	H	CH_3	H	CH_3	CH	CH	c-C_3H_5
333	CH_2-c-C_3H_5	H	CH_3	H	CH_3	CH	CH	c-C_3H_5
334	$CH_2CH_2CH_3$	H	CH_3	H	CH_3	CH	CH	c-C_3H_5

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
335	CH_3	CH_3	H	CH_3	CH_3	CH	CH	c-C_3H_5
336	$CH_2CH=CH_2$	CH_3	H	CH_3	CH_3	CH	CH	c-C_3H_5
337	CH_2-c-C_3H_5	CH_3	H	CH_3	CH_3	CH	CH	c-C_3H_5
338	$CH_2CH_2CH_3$	CH_3	H	CH_3	CH_3	CH	CH	c-C_3H_5
339	CH_3	CH_3	CH_3	H	CH_3	CH	CH	c-C_3H_5
340	$CH_2CH=CH_2$	CH_3	CH_3	H	CH_3	CH	CH	c-C_3H_5
341	CH_2-c-C_3H_5	CH_3	CH_3	H	CH_3	CH	CH	c-C_3H_5
342	$CH_2CH_2CH_3$	CH_3	CH_3	H	CH_3	CH	CH	c-C_3H_5
343	(s)$(CH_2)_3$		H	H	CH_3	CH	CH	c-C_3H_5
344	(s)$(CH_2)_4$		H	H	CH_3	CH	CH	c-C_3H_5
345	*rac*$(CH_2)_3$		H	H	CH_3	CH	CH	c-C_3H_5
346	*rac*$(CH_2)_4$		H	H	CH_3	CH	CH	c-C_3H_5
347	(R)$(CH_2)_3$		H	H	CH_3	CH	CH	c-C_3H_5
348	(R)$(CH_2)_4$		H	H	CH_3	CH	CH	c-C_3H_5
349	$CH_2CH=CH_2$	H	H	H	H	CH	C-Cl	c-C_3H_5
350	CH_2-c-C_3H_5	H	H	H	H	CH	C-Cl	c-C_3H_5
351	$CH_2CH_2CH_3$	H	H	H	H	CH	C-Cl	c-C_3H_5
352	$CH_2CH=CH_2$	(s)CH_3	H	H	H	CH	C-Cl	c-C_3H_5
353	CH_2-c-C_3H_5	(s)CH_3	H	H	H	CH	C-Cl	c-C_3H_5
354	CH_2CH_3	(s)CH_3	H	H	H	CH	C-Cl	c-C_3H_5
355	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	CH	C-Cl	c-C_3H_5
356	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	CH	C-Cl	c-C_3H_5
357	CH_2-c-C_3H_5	*rac*- CH_3	H	H	H	CH	C-Cl	c-C_3H_5
358	CH_2CH_3	*rac*- CH_3	H	H	H	CH	C-Cl	c-C_3H_5
359	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	CH	C-Cl	c-C_3H_5
360	$CH_2CH=CH_2$	(R)CH_3	H	H	H	CH	C-Cl	c-C_3H_5
361	CH_2-c-C_3H_5	(R)CH_3	H	H	H	CH	C-Cl	c-C_3H_5
362	CH_2CH_3	(R)CH_3	H	H	H	CH	C-Cl	c-C_3H_5
363	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	CH	C-Cl	c-C_3H_5
364	$CH_2CH=CH_2$	H	H	H	CH_3	CH	C-Cl	c-C_3H_5
365	CH_2-c-C_3H_5	H	H	H	CH_3	CH	C-Cl	c-C_3H_5
366	$CH_2CH_2CH_3$	H	H	H	CH_3	CH	C-Cl	c-C_3H_5
367	$CH_2CH=CH_2$	(s)CH_3	H	H	CH_3	CH	C-Cl	c-C_3H_5
368	CH_2-c-C_3H_5	(s)CH_3	H	H	CH_3	CH	C-Cl	c-C_3H_5
369	CH_2CH_3	(s)CH_3	H	H	CH_3	CH	C-Cl	c-C_3H_5
370	$CH_2CH_2CH_3$	(s)CH_3	H	H	CH_3	CH	C-Cl	c-C_3H_5
371	$CH_2CH=CH_2$	*rac*- CH_3	H	H	CH_3	CH	C-Cl	c-C_3H_5
372	CH_2-c-C_3H_5	*rac*- CH_3	H	H	CH_3	CH	C-Cl	c-C_3H_5
373	CH_2CH_3	*rac*- CH_3	H	H	CH_3	CH	C-Cl	c-C_3H_5
374	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	CH_3	CH	C-Cl	c-C_3H_5
375	$CH_2CH=CH_2$	(R)CH_3	H	H	CH_3	CH	C-Cl	c-C_3H_5
376	CH_2-c-C_3H_5	(R)CH_3	H	H	CH_3	CH	C-Cl	c-C_3H_5

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
377	$CH_2CH_2CH_3$	(R)CH_3	H	H	CH_3	CH	C-Cl	c-C_3H_5
378	CH_2CH_3	(R)CH_3	H	H	CH_3	CH	C-Cl	c-C_3H_5
379	$CH_2CH=CH_2$	H	H	H	H	CH	C-CH_3	c-C_3H_5
380	CH_2-c-C_3H_5	H	H	H	H	CH	C-CH_3	c-C_3H_5
381	$CH_2CH_2CH_3$	H	H	H	H	CH	C-CH_3	c-C_3H_5
382	$CH_2CH=CH_2$	(s)CH_3	H	H	H	CH	C-CH_3	c-C_3H_5
383	CH_2-c-C_3H_5	(s)CH_3	H	H	H	CH	C-CH_3	c-C_3H_5
384	CH_2CH_3	(s)CH_3	H	H	H	CH	C-CH_3	c-C_3H_5
385	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	CH	C-CH_3	c-C_3H_5
386	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	CH	C-CH_3	c-C_3H_5
387	CH_2-c-C_3H_5	*rac*- CH_3	H	H	H	CH	C-CH_3	c-C_3H_5
388	CH_2CH_3	*rac*- CH_3	H	H	H	CH	C-CH_3	c-C_3H_5
389	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	CH	C-CH_3	c-C_3H_5
390	$CH_2CH=CH_2$	(R)CH_3	H	H	H	CH	C-CH_3	c-C_3H_5
391	CH_2-c-C_3H_5	(R)CH_3	H	H	H	CH	C-CH_3	c-C_3H_5
392	CH_2CH_3	(R)CH_3	H	H	H	CH	C-CH_3	c-C_3H_5
393	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	CH	C-CH_3	c-C_3H_5
394	$CH_2CH=CH_2$	H	H	H	CH_3	CH	C-CH_3	c-C_3H_5
395	CH_2-c-C_3H_5	H	H	H	CH_3	CH	C-CH_3	c-C_3H_5
396	$CH_2CH_2CH_3$	H	H	H	CH_3	CH	C-CH_3	c-C_3H_5
397	$CH_2CH=CH_2$	(s)CH_3	H	H	CH_3	CH	C-CH_3	c-C_3H_5
398	CH_2-c-C_3H_5	(s)CH_3	H	H	CH_3	CH	C-CH_3	c-C_3H_5
399	$CH_2CH_2CH_3$	(s)CH_3	H	H	CH_3	CH	C-CH_3	c-C_3H_5
400	$CH_2CH=CH_2$	*rac*- CH_3	H	H	CH_3	CH	C-CH_3	c-C_3H_5
401	CH_2-c-C_3H_5	*rac*- CH_3	H	H	CH_3	CH	C-CH_3	c-C_3H_5
402	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	CH_3	CH	C-CH_3	c-C_3H_5
403	$CH_2CH=CH_2$	(R)CH_3	H	H	CH_3	CH	C-CH_3	c-C_3H_5
404	CH_2-c-C_3H_5	(R)CH_3	H	H	CH_3	CH	C-CH_3	c-C_3H_5
405	$CH_2CH_2CH_3$	(R)CH_3	H	H	CH_3	CH	C-CH_3	c-C_3H_5
406	$CH_2CH=CH_2$	H	H	H	H	C-Cl	CH	c-C_3H_5
407	CH_2-c-C_3H_5	H	H	H	H	C-Cl	CH	c-C_3H_5
408	$CH_2CH_2CH_3$	H	H	H	H	C-Cl	CH	c-C_3H_5
409	$CH_2CH=CH_2$	(s)CH_3	H	H	H	C-Cl	CH	c-C_3H_5
410	CH_2-c-C_3H_5	(s)CH_3	H	H	H	C-Cl	CH	c-C_3H_5
411	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	C-Cl	CH	c-C_3H_5
412	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	C-Cl	CH	c-C_3H_5
413	CH_2-c-C_3H_5	*rac*- CH_3	H	H	H	C-Cl	CH	c-C_3H_5
414	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	C-Cl	CH	c-C_3H_5
415	$CH_2CH=CH_2$	H	H	H	CH_3	C-Cl	CH	c-C_3H_5
416	CH_2-c-C_3H_5	H	H	H	CH_3	C-Cl	CH	c-C_3H_5
417	$CH_2CH_2CH_3$	H	H	H	CH_3	C-Cl	CH	c-C_3H_5
418	$CH_2CH=CH_2$	(s)CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
419	CH_2-c-C_3H_5	(s)CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5
420	CH_2CH_3	(s)CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5
421	$CH_2CH_2CH_3$	(s)CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5
422	$CH_2CH=CH_2$	*rac*- CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5
423	CH_2-c-C_3H_5	*rac*- CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5
424	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5
425	$CH_2CH=CH_2$	(R)CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5
426	CH_2-c-C_3H_5	(R)CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5
427	CH_2CH_3	(R)CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5
428	$CH_2CH_2CH_3$	(R)CH_3	H	H	CH_3	C-Cl	CH	c-C_3H_5
429	$CH_2CH=CH_2$	H	H	H	H	C-CH_3	CH	c-C_3H_5
430	CH_2-c-C_3H_5	H	H	H	H	C-CH_3	CH	c-C_3H_5
431	$CH_2CH_2CH_3$	H	H	H	H	C-CH_3	CH	c-C_3H_5
432	$CH_2CH=CH_2$	(s)CH_3	H	H	H	C-CH_3	CH	c-C_3H_5
433	CH_2-c-C_3H_5	(s)CH_3	H	H	H	C-CH_3	CH	c-C_3H_5
434	CH_2CH_3	(s)CH_3	H	H	H	C-CH_3	CH	c-C_3H_5
435	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	C-CH_3	CH	c-C_3H_5
436	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	C-CH_3	CH	c-C_3H_5
437	CH_2-c-C_3H_5	*rac*- CH_3	H	H	H	C-CH_3	CH	c-C_3H_5
438	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	C-CH_3	CH	c-C_3H_5
439	$CH_2CH=CH_2$	(R)CH_3	H	H	H	C-CH_3	CH	c-C_3H_5
440	CH_2-c-C_3H_5	(R)CH_3	H	H	H	C-CH_3	CH	c-C_3H_5
441	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	C-CH_3	CH	c-C_3H_5
442	$CH_2CH=CH_2$	H	H	H	CH_3	C-CH_3	CH	c-C_3H_5
443	CH_2-c-C_3H_5	H	H	H	CH_3	C-CH_3	CH	c-C_3H_5
444	$CH_2CH_2CH_3$	H	H	H	CH_3	C-CH_3	CH	c-C_3H_5
445	$CH_2CH=CH_2$	(s)CH_3	H	H	CH_3	C-CH_3	CH	c-C_3H_5
446	CH_2-c-C_3H_5	(s)CH_3	H	H	CH_3	C-CH_3	CH	c-C_3H_5
447	$CH_2CH_2CH_3$	(s)CH_3	H	H	CH_3	C-CH_3	CH	c-C_3H_5
448	$CH_2CH=CH_2$	*rac*- CH_3	H	H	CH_3	C-CH_3	CH	c-C_3H_5
449	CH_2-c-C_3H_5	*rac*- CH_3	H	H	CH_3	C-CH_3	CH	c-C_3H_5
450	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	CH_3	C-CH_3	CH	c-C_3H_5
451	H	H	H	H	H	CH	CH	C_2H_5
452	CH_3	H	H	H	H	CH	CH	C_2H_5
453	CH_2CH_3	H	H	H	H	CH	CH	C_2H_5
454	$CH_2CH=CH_2$	H	H	H	H	CH	CH	C_2H_5
455	CH_2-c-C_3H_5	H	H	H	H	CH	CH	C_2H_5
456	$CH_2CH_2CH_3$	H	H	H	H	CH	CH	C_2H_5
457	H	(s)CH_3	H	H	H	CH	CH	C_2H_5
458	CH_3	(s)CH_3	H	H	H	CH	CH	C_2H_5
459	CH_2CH_3	(s)CH_3	H	H	H	CH	CH	C_2H_5
460	$CH_2CH=CH_2$	(s)CH_3	H	H	H	CH	CH	C_2H_5

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
461	CH_2-c-C_3H_5	(s)CH_3	H	H	H	CH	CH	C_2H_5
462	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	CH	CH	C_2H_5
463	CH_3	*rac*- CH_3	H	H	H	CH	CH	C_2H_5
464	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	CH	CH	C_2H_5
465	CH_2-c-C_3H_5	*rac*- CH_3	H	H	H	CH	CH	C_2H_5
466	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	CH	CH	C_2H_5
467	CH_3	(R)CH_3	H	H	H	CH	CH	C_2H_5
468	CH_2CH_3	(R)CH_3	H	H	H	CH	CH	C_2H_5
469	$CH_2CH=CH_2$	(R)CH_3	H	H	H	CH	CH	C_2H_5
470	CH_2-c-C_3H_5	(R)CH_3	H	H	H	CH	CH	C_2H_5
471	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	CH	CH	C_2H_5
472	CH_3	H	CH_3	H	H	CH	CH	C_2H_5
473	$CH_2CH=CH_2$	H	CH_3	H	H	CH	CH	C_2H_5
474	CH_2-c-C_3H_5	H	CH_3	H	H	CH	CH	C_2H_5
475	$CH_2CH_2CH_3$	H	CH_3	H	H	CH	CH	C_2H_5
476	CH_3	CH_3	H	CH_3	H	CH	CH	C_2H_5
477	$CH_2CH=CH_2$	CH_3	H	CH_3	H	CH	CH	C_2H_5
478	CH_2-c-C_3H_5	CH_3	H	CH_3	H	CH	CH	C_2H_5
479	$CH_2CH_2CH_3$	CH_3	H	CH_3	H	CH	CH	C_2H_5
480	CH_3	CH_3	CH_3	H	H	CH	CH	C_2H_5
481	$CH_2CH=CH_2$	CH_3	CH_3	H	H	CH	CH	C_2H_5
482	CH_2-c-C_3H_5	CH_3	CH_3	H	H	CH	CH	C_2H_5
483	$CH_2CH_2CH_3$	CH_3	CH_3	H	H	CH	CH	C_2H_5
484	(s)$(CH_2)_3$		H	H	H	CH	CH	C_2H_5
485	(s)$(CH_2)_4$		H	H	H	CH	CH	C_2H_5
486	rac$(CH_2)_3$		H	H	H	CH	CH	C_2H_5
487	rac$(CH_2)_4$		H	H	H	CH	CH	C_2H_5
488	(R)$(CH_2)_3$		H	H	H	CH	CH	C_2H_5
489	(R)$(CH_2)_4$		H	H	H	CH	CH	C_2H_5
490	CH_3	H	H	H	CH_3	CH	CH	C_2H_5
491	$CH_2CH=CH_2$	H	H	H	CH_3	CH	CH	C_2H_5
492	CH_2-c-C_3H_5	H	H	H	CH_3	CH	CH	C_2H_5
493	$CH_2CH_2CH_3$	H	H	H	CH_3	CH	CH	C_2H_5
494	CH_3	(s)CH_3	H	H	CH_3	CH	CH	C_2H_5
495	$CH_2CH=CH_2$	(s)CH_3	H	H	CH_3	CH	CH	C_2H_5
496	CH_2-c-C_3H_5	(s)CH_3	H	H	CH_3	CH	CH	C_2H_5
497	CH_2CH_3	(s)CH_3	H	H	CH_3	CH	CH	C_2H_5
498	$CH_2CH_2CH_3$	(s)CH_3	H	H	CH_3	CH	CH	C_2H_5
499	$CH_2CH=CH_2$	*rac*- CH_3	H	H	CH_3	CH	CH	C_2H_5
500	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	CH_3	CH	CH	C_2H_5
501	CH_3	(R)CH_3	H	H	CH_3	CH	CH	C_2H_5
502	$CH_2CH=CH_2$	(R)CH_3	H	H	CH_3	CH	CH	C_2H_5

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
503	CH_2-c-C_3H_5	(R)CH_3	H	H	CH_3	CH	CH	C_2H_5
504	$CH_2CH=CH_2$	H	CH_3	H	CH_3	CH	CH	C_2H_5
505	$CH_2CH_2CH_3$	H	CH_3	H	CH_3	CH	CH	C_2H_5
506	$CH_2CH=CH_2$	CH_3	H	CH_3	CH_3	CH	CH	C_2H_5
507	$CH_2CH_2CH_3$	CH_3	H	CH_3	CH_3	CH	CH	C_2H_5
508	$CH_2CH=CH_2$	CH_3	CH_3	H	CH_3	CH	CH	C_2H_5
509	$CH_2CH_2CH_3$	CH_3	CH_3	H	CH_3	CH	CH	C_2H_5
510	(s)$(CH_2)_3$		H	H	CH_3	CH	CH	C_2H_5
511	(s)$(CH_2)_4$		H	H	CH_3	CH	CH	C_2H_5
512	*rac*$(CH_2)_3$		H	H	CH_3	CH	CH	C_2H_5
513	*rac*$(CH_2)_4$		H	H	CH_3	CH	CH	C_2H_5
514	H	H	H	H	H	CH	CH	CH_3
515	CH_3	H	H	H	H	CH	CH	CH_3
516	CH_2CH_3	H	H	H	H	CH	CH	CH_3
517	$CH_2CH=CH_2$	H	H	H	H	CH	CH	CH_3
518	CH_2-c-C_3H_5	H	H	H	H	CH	CH	CH_3
519	$CH_2CH_2CH_3$	H	H	H	H	CH	CH	CH_3
520	H	(s)CH_3	H	H	H	CH	CH	CH_3
521	CH_3	(s)CH_3	H	H	H	CH	CH	CH_3
522	CH_2CH_3	(s)CH_3	H	H	H	CH	CH	CH_3
523	$CH_2CH=CH_2$	(s)CH_3	H	H	H	CH	CH	CH_3
524	CH_2-c-C_3H_5	(s)CH_3	H	H	H	CH	CH	CH_3
525	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	CH	CH	CH_3
526	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	CH	CH	CH_3
527	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	CH	CH	CH_3
528	CH_2CH_3	(R)CH_3	H	H	H	CH	CH	CH_3
529	$CH_2CH=CH_2$	(R)CH_3	H	H	H	CH	CH	CH_3
530	CH_2-c-C_3H_5	(R)CH_3	H	H	H	CH	CH	CH_3
531	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	CH	CH	CH_3
532	$CH_2CH=CH_2$	H	CH_3	H	H	CH	CH	CH_3
533	$CH_2CH_2CH_3$	H	CH_3	H	H	CH	CH	CH_3
534	$CH_2CH=CH_2$	CH_3	H	CH_3	H	CH	CH	CH_3
535	$CH_2CH_2CH_3$	CH_3	H	CH_3	H	CH	CH	CH_3
536	$CH_2CH=CH_2$	CH_3	CH_3	H	H	CH	CH	CH_3
537	$CH_2CH_2CH_3$	CH_3	CH_3	H	H	CH	CH	CH_3
538	(s)$(CH_2)_3$		H	H	H	CH	CH	CH_3
539	(s)$(CH_2)_4$		H	H	H	CH	CH	CH_3
540	rac$(CH_2)_3$		H	H	H	CH	CH	CH_3
541	rac$(CH_2)_4$		H	H	H	CH	CH	CH_3
542	(R)$(CH_2)_3$		H	H	H	CH	CH	CH_3
543	(R)$(CH_2)_4$		H	H	H	CH	CH	CH_3
544	H	H	H	H	CH_3	CH	CH	$CH=CH_2$

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
545	CH_3	H	H	H	CH_3	CH	CH	$CH=CH_2$
546	CH_2CH_3	H	H	H	CH_3	CH	CH	$CH=CH_2$
547	$CH_2CH=CH_2$	H	H	H	CH_3	CH	CH	$CH=CH_2$
548	CH_2-c-C_3H_5	H	H	H	CH_3	CH	CH	$CH=CH_2$
549	$CH_2CH_2CH_3$	H	H	H	CH_3	CH	CH	$CH=CH_2$
550	H	(s)CH_3	H	H	CH_3	CH	CH	$CH=CH_2$
551	CH_3	(s)CH_3	H	H	CH_3	CH	CH	$CH=CH_2$
552	CH_2CH_3	(s)CH_3	H	H	CH_3	CH	CH	$CH=CH_2$
553	$CH_2CH=CH_2$	(s)CH_3	H	H	CH_3	CH	CH	$CH=CH_2$
554	CH_2-c-C_3H_5	(s)CH_3	H	H	CH_3	CH	CH	$CH=CH_2$
555	$CH_2CH_2CH_3$	(s)CH_3	H	H	CH_3	CH	CH	$CH=CH_2$
556	$CH_2CH=CH_2$	*rac*- CH_3	H	H	CH_3	CH	CH	$CH=CH_2$
557	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	CH_3	CH	CH	$CH=CH_2$
558	CH_2CH_3	(s)CH_3	H	H	CH_3	CH	CH	$CH=CH_2$
559	$CH_2CH=CH_2$	(R)CH_3	H	H	CH_3	CH	CH	$CH=CH_2$
560	CH_2-c-C_3H_5	(R)CH_3	H	H	CH_3	CH	CH	$CH=CH_2$
561	$CH_2CH_2CH_3$	(R)CH_3	H	H	CH_3	CH	CH	$CH=CH_2$
562	$CH_2CH=CH_2$	H	CH_3	H	CH_3	CH	CH	$CH=CH_2$
563	$CH_2CH_2CH_3$	H	CH_3	H	CH_3	CH	CH	$CH=CH_2$
564	$CH_2CH=CH_2$	CH_3	H	CH_3	CH_3	CH	CH	$CH=CH_2$
565	$CH_2CH_2CH_3$	CH_3	H	CH_3	CH_3	CH	CH	$CH=CH_2$
566	$CH_2CH=CH_2$	CH_3	CH_3	H	CH_3	CH	CH	$CH=CH_2$
567	$CH_2CH_2CH_3$	CH_3	CH_3	H	CH_3	CH	CH	$CH=CH_2$
568	$(CH_2)_3$		H	H	CH_3	CH	CH	$CH=CH_2$
569	$(CH_2)_4$		H	H	CH_3	CH	CH	$CH=CH_2$
570	H	H	H	H	H	N	CH	$CH(CH_3)_2$
571	CH_3	H	H	H	H	N	CH	$CH(CH_3)_2$
572	CH_2CH_3	H	H	H	H	N	CH	$CH(CH_3)_2$
573	$CH_2CH=CH_2$	H	H	H	H	N	CH	$CH(CH_3)_2$
574	CH_2-c-C_3H_5	H	H	H	H	N	CH	$CH(CH_3)_2$
575	$CH_2CH_2CH_3$	H	H	H	H	N	CH	$CH(CH_3)_2$
576	H	(s)CH_3	H	H	H	N	CH	$CH(CH_3)_2$
577	CH_3	(s)CH_3	H	H	H	N	CH	$CH(CH_3)_2$
578	CH_2CH_3	(s)CH_3	H	H	H	N	CH	$CH(CH_3)_2$
579	$CH_2CH=CH_2$	(s)CH_3	H	H	H	N	CH	$CH(CH_3)_2$
580	CH_2-c-C_3H_5	(s)CH_3	H	H	H	N	CH	$CH(CH_3)_2$
581	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	N	CH	$CH(CH_3)_2$
582	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	N	CH	$CH(CH_3)_2$
583	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	N	CH	$CH(CH_3)_2$
584	CH_2CH_3	(R)CH_3	H	H	H	N	CH	$CH(CH_3)_2$
585	$CH_2CH=CH_2$	(R)CH_3	H	H	H	N	CH	$CH(CH_3)_2$
586	CH_2-c-C_3H_5	(R)CH_3	H	H	H	N	CH	$CH(CH_3)_2$

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
587	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	N	CH	$CH(CH_3)_2$
588	(s)$(CH_2)_3$		H	H	H	N	CH	$CH(CH_3)_2$
589	(s)$(CH_2)_4$		H	H	H	N	CH	$CH(CH_3)_2$
590	*rac*$(CH_2)_3$		H	H	H	N	CH	$CH(CH_3)_2$
591	*rac*$(CH_2)_4$		H	H	H	N	CH	$CH(CH_3)_2$
592	(R)$(CH_2)_3$		H	H	H	N	CH	$CH(CH_3)_2$
593	(R)$(CH_2)_4$		H	H	H	N	CH	$CH(CH_3)_2$
594	H	H	H	H	H	N	CH	$CH=CH_2$
595	CH_3	H	H	H	H	N	CH	$CH=CH_2$
596	CH_2CH_3	H	H	H	H	N	CH	$CH=CH_2$
597	$CH_2CH=CH_2$	H	H	H	H	N	CH	$CH=CH_2$
598	CH_2-c-C_3H_5	H	H	H	H	N	CH	$CH=CH_2$
599	$CH_2CH_2CH_3$	H	H	H	H	N	CH	$CH=CH_2$
600	H	(s)CH_3	H	H	H	N	CH	$CH=CH_2$
601	CH_3	(s)CH_3	H	H	H	N	CH	$CH=CH_2$
602	CH_2CH_3	(s)CH_3	H	H	H	N	CH	$CH=CH_2$
603	$CH_2CH=CH_2$	(s)CH_3	H	H	H	N	CH	$CH=CH_2$
604	CH_2-c-C_3H_5	(s)CH_3	H	H	H	N	CH	$CH=CH_2$
605	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	N	CH	$CH=CH_2$
606	$CH_2CH=CH_2$	(R)CH_3	H	H	H	N	CH	$CH=CH_2$
607	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	N	CH	$CH=CH_2$
608	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	N	CH	$CH=CH_2$
609	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	N	CH	$CH=CH_2$
610	H	H	H	H	H	N	CH	c-C_3H_5
611	CH_3	H	H	H	H	N	CH	c-C_3H_5
612	CH_2CH_3	H	H	H	H	N	CH	c-C_3H_5
613	$CH_2CH=CH_2$	H	H	H	H	N	CH	c-C_3H_5
614	CH_2-c-C_3H_5	H	H	H	H	N	CH	c-C_3H_5
615	$CH_2CH_2CH_3$	H	H	H	H	N	CH	c-C_3H_5
616	H	(s)CH_3	H	H	H	N	CH	c-C_3H_5
617	CH_3	(s)CH_3	H	H	H	N	CH	c-C_3H_5
618	CH_2CH_3	(s)CH_3	H	H	H	N	CH	c-C_3H_5
619	$CH_2CH=CH_2$	(s)CH_3	H	H	H	N	CH	c-C_3H_5
620	CH_2-c-C_3H_5	(s)CH_3	H	H	H	N	CH	c-C_3H_5
621	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	N	CH	c-C_3H_5
622	CH_2CH_3	(R)CH_3	H	H	H	N	CH	c-C_3H_5
623	$CH_2CH=CH_2$	(R)CH_3	H	H	H	N	CH	c-C_3H_5
624	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	N	CH	c-C_3H_5
625	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	N	CH	c-C_3H_5
626	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	N	CH	c-C_3H_5
627	H	H	H	H	H	N	CH	CH_3
628	CH_3	H	H	H	H	N	CH	CH_3

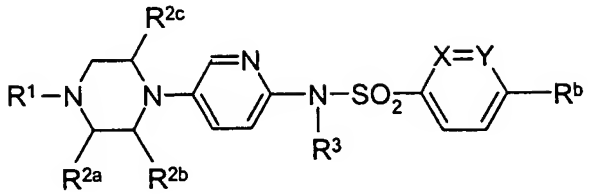
No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
629	CH_2CH_3	H	H	H	H	N	CH	CH_3
630	$CH_2CH=CH_2$	H	H	H	H	N	CH	CH_3
631	CH_2-c-C_3H_5	H	H	H	H	N	CH	CH_3
632	$CH_2CH_2CH_3$	H	H	H	H	N	CH	CH_3
633	H	(s)CH_3	H	H	H	N	CH	CH_3
634	CH_3	(s)CH_3	H	H	H	N	CH	CH_3
635	CH_2CH_3	(s)CH_3	H	H	H	N	CH	CH_3
636	$CH_2CH=CH_2$	(s)CH_3	H	H	H	N	CH	CH_3
637	CH_2-c-C_3H_5	(s)CH_3	H	H	H	N	CH	CH_3
638	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	N	CH	CH_3
639	$CH_2CH=CH_2$	(R)CH_3	H	H	H	N	CH	CH_3
640	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	N	CH	CH_3
641	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	N	CH	CH_3
642	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	N	CH	CH_3
643	H	H	H	H	H	N	CH	CF_3
644	CH_3	H	H	H	H	N	CH	CF_3
645	CH_2CH_3	H	H	H	H	N	CH	CF_3
646	$CH_2CH=CH_2$	H	H	H	H	N	CH	CF_3
647	CH_2-c-C_3H_5	H	H	H	H	N	CH	CF_3
648	$CH_2CH_2CH_3$	H	H	H	H	N	CH	CF_3
649	H	(s)CH_3	H	H	H	N	CH	CF_3
650	CH_3	(s)CH_3	H	H	H	N	CH	CF_3
651	CH_2CH_3	(s)CH_3	H	H	H	N	CH	CF_3
652	$CH_2CH=CH_2$	(s)CH_3	H	H	H	N	CH	CF_3
653	CH_2-c-C_3H_5	(s)CH_3	H	H	H	N	CH	CF_3
654	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	N	CH	CF_3
655	$CH_2CH=CH_2$	(R)CH_3	H	H	H	N	CH	CF_3
656	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	N	CH	CF_3
657	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	N	CH	CF_3
658	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	N	CH	CF_3
659	H	H	H	H	H	CH	N	$CH(CH_3)_2$
660	CH_3	H	H	H	H	CH	N	$CH(CH_3)_2$
661	CH_2CH_3	H	H	H	H	CH	N	$CH(CH_3)_2$
662	$CH_2CH=CH_2$	H	H	H	H	CH	N	$CH(CH_3)_2$
663	CH_2-c-C_3H_5	H	H	H	H	CH	N	$CH(CH_3)_2$
664	$CH_2CH_2CH_3$	H	H	H	H	CH	N	$CH(CH_3)_2$
665	H	(s)CH_3	H	H	H	CH	N	$CH(CH_3)_2$
666	CH_3	(s)CH_3	H	H	H	CH	N	$CH(CH_3)_2$
667	CH_2CH_3	(s)CH_3	H	H	H	CH	N	$CH(CH_3)_2$
668	$CH_2CH=CH_2$	(s)CH_3	H	H	H	CH	N	$CH(CH_3)_2$
669	CH_2-c-C_3H_5	(s)CH_3	H	H	H	CH	N	$CH(CH_3)_2$
670	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	CH	N	$CH(CH_3)_2$

No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
671	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	CH	N	$CH(CH_3)_2$
672	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	CH	N	$CH(CH_3)_2$
673	CH_2CH_3	(R)CH_3	H	H	H	CH	N	$CH(CH_3)_2$
674	$CH_2CH=CH_2$	(R)CH_3	H	H	H	CH	N	$CH(CH_3)_2$
675	CH_2-c-C_3H_5	(R)CH_3	H	H	H	CH	N	$CH(CH_3)_2$
676	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	CH	N	$CH(CH_3)_2$
677	H	H	H	H	H	CH	N	$CH=CH_2$
678	CH_3	H	H	H	H	CH	N	$CH=CH_2$
679	CH_2CH_3	H	H	H	H	CH	N	$CH=CH_2$
680	$CH_2CH=CH_2$	H	H	H	H	CH	N	$CH=CH_2$
681	CH_2-c-C_3H_5	H	H	H	H	CH	N	$CH=CH_2$
682	$CH_2CH_2CH_3$	H	H	H	H	CH	N	$CH=CH_2$
683	H	(s)CH_3	H	H	H	CH	N	$CH=CH_2$
684	CH_3	(s)CH_3	H	H	H	CH	N	$CH=CH_2$
685	CH_2CH_3	(s)CH_3	H	H	H	CH	N	$CH=CH_2$
686	$CH_2CH=CH_2$	(s)CH_3	H	H	H	CH	N	$CH=CH_2$
687	CH_2-c-C_3H_5	(s)CH_3	H	H	H	CH	N	$CH=CH_2$
688	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	CH	N	$CH=CH_2$
689	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	CH	N	$CH=CH_2$
690	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	CH	N	$CH=CH_2$
691	CH_2CH_3	(R)CH_3	H	H	H	CH	N	$CH=CH_2$
692	$CH_2CH=CH_2$	(R)CH_3	H	H	H	CH	N	$CH=CH_2$
693	CH_2-c-C_3H_5	(R)CH_3	H	H	H	CH	N	$CH=CH_2$
694	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	CH	N	$CH=CH_2$
695	H	H	H	H	H	CH	N	c-C_3H_5
696	CH_3	H	H	H	H	CH	N	c-C_3H_5
697	CH_2CH_3	H	H	H	H	CH	N	c-C_3H_5
698	$CH_2CH=CH_2$	H	H	H	H	CH	N	c-C_3H_5
699	CH_2-c-C_3H_5	H	H	H	H	CH	N	c-C_3H_5
700	$CH_2CH_2CH_3$	H	H	H	H	CH	N	c-C_3H_5
701	H	(s)CH_3	H	H	H	CH	N	c-C_3H_5
702	CH_3	(s)CH_3	H	H	H	CH	N	c-C_3H_5
703	CH_2CH_3	(s)CH_3	H	H	H	CH	N	c-C_3H_5
704	$CH_2CH=CH_2$	(s)CH_3	H	H	H	CH	N	c-C_3H_5
705	CH_2-c-C_3H_5	(s)CH_3	H	H	H	CH	N	c-C_3H_5
706	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	CH	N	c-C_3H_5
707	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	CH	N	c-C_3H_5
708	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	CH	N	c-C_3H_5
709	CH_2CH_3	(R)CH_3	H	H	H	CH	N	c-C_3H_5
710	$CH_2CH=CH_2$	(R)CH_3	H	H	H	CH	N	c-C_3H_5
711	CH_2-c-C_3H_5	(R)CH_3	H	H	H	CH	N	c-C_3H_5
712	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	CH	N	c-C_3H_5

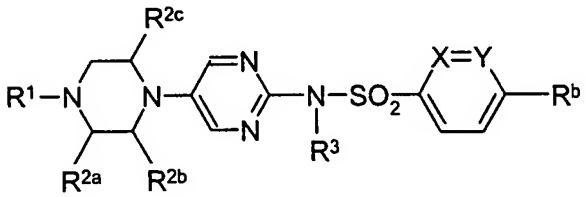
No.	R^1	R^{2a}	R^{2b}	R^{2c}	R^3	X	Y	R^b
713	H	H	H	H	H	CH	N	CH_3
714	CH_3	H	H	H	H	CH	N	CH_3
715	CH_2CH_3	H	H	H	H	CH	N	CH_3
716	$CH_2CH=CH_2$	H	H	H	H	CH	N	CH_3
717	CH_2-c-C_3H_5	H	H	H	H	CH	N	CH_3
718	$CH_2CH_2CH_3$	H	H	H	H	CH	N	CH_3
719	H	(s)CH_3	H	H	H	CH	N	CH_3
720	CH_3	(s)CH_3	H	H	H	CH	N	CH_3
721	CH_2CH_3	(s)CH_3	H	H	H	CH	N	CH_3
722	$CH_2CH=CH_2$	(s)CH_3	H	H	H	CH	N	CH_3
723	CH_2-c-C_3H_5	(s)CH_3	H	H	H	CH	N	CH_3
724	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	CH	N	CH_3
725	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	CH	N	CH_3
726	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	CH	N	CH_3
727	CH_2CH_3	(R)CH_3	H	H	H	CH	N	CH_3
728	$CH_2CH=CH_2$	(R)CH_3	H	H	H	CH	N	CH_3
729	CH_2-c-C_3H_5	(R)CH_3	H	H	H	CH	N	CH_3
730	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	CH	N	CH_3
731	H	H	H	H	H	CH	N	CF_3
732	CH_3	H	H	H	H	CH	N	CF_3
733	CH_2CH_3	H	H	H	H	CH	N	CF_3
734	$CH_2CH=CH_2$	H	H	H	H	CH	N	CF_3
735	CH_2-c-C_3H_5	H	H	H	H	CH	N	CF_3
736	$CH_2CH_2CH_3$	H	H	H	H	CH	N	CF_3
737	H	(s)CH_3	H	H	H	CH	N	CF_3
738	CH_3	(s)CH_3	H	H	H	CH	N	CF_3
739	CH_2CH_3	(s)CH_3	H	H	H	CH	N	CF_3
740	$CH_2CH=CH_2$	(s)CH_3	H	H	H	CH	N	CF_3
741	CH_2-c-C_3H_5	(s)CH_3	H	H	H	CH	N	CF_3
742	$CH_2CH_2CH_3$	(s)CH_3	H	H	H	CH	N	CF_3
743	CH_2CH_3	(R)CH_3	H	H	H	CH	N	CF_3
744	$CH_2CH=CH_2$	(R)CH_3	H	H	H	CH	N	CF_3
745	CH_2-c-C_3H_5	(R)CH_3	H	H	H	CH	N	CF_3
746	$CH_2CH_2CH_3$	(R)CH_3	H	H	H	CH	N	CF_3
747	$CH_2CH=CH_2$	*rac*- CH_3	H	H	H	CH	N	CF_3
748	$CH_2CH_2CH_3$	*rac*- CH_3	H	H	H	CH	N	CF_3

rac: racemate; (S): S configuration; (R) R configuration.

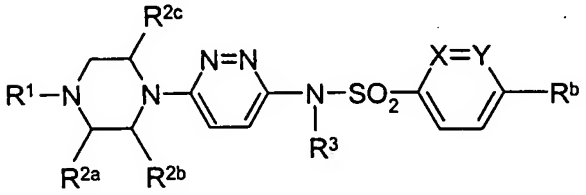
Other examples of compounds according to the invention are the compounds of the general formulae Ia.3, Ib, Ic, Id, Ie and If:



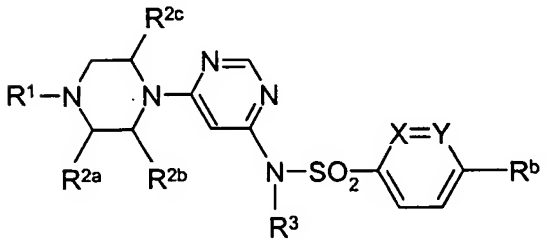
(Ia.3)



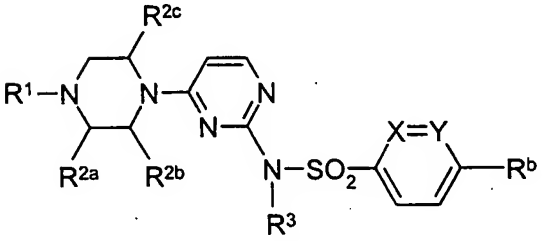
(Ib)



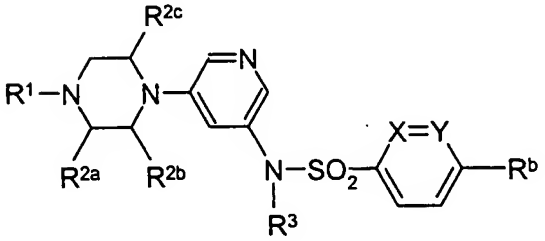
(Ic)



(Id)



(Ie)

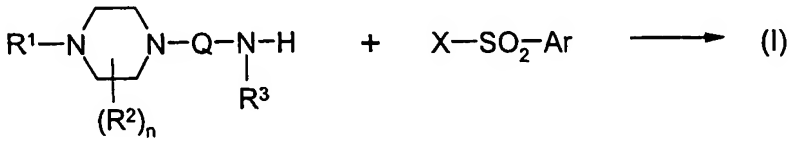


(If)

in which R^1, R^{2a}, R^{2b}, R^{2c}, R^3, X, Y and R^b have the meanings specified in one line in Table 1.

The compounds I according to the invention are prepared in analogy with methods known from the literature. An important approach to the compounds according to the invention is offered by the reaction of a hetarylamine II with an arylsulfonic acid derivative III as depicted in scheme 1.

Scheme 1:



(II) (III)

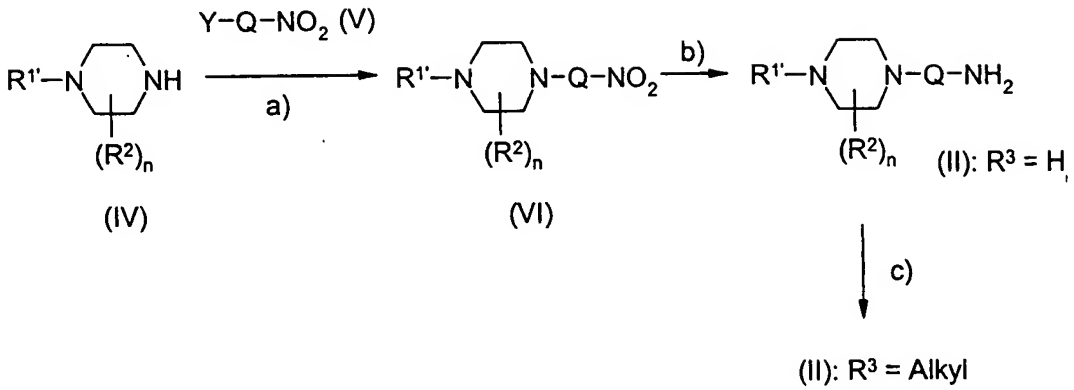
In scheme 1, n, R^1, R^2, R^3, Ar and Q have the previously mentioned meanings. X is a nucleophilically displaceable leaving group, in particular a halogen atom and, especially, chlorine or bromine. The reaction depicted in scheme 1 takes place under the reaction conditions which are customary for preparing arylsulfonamide compounds and which are described, for example, in European J. Org. Chem. 2002 (13), pp. 2094-2108, Tetrahedron 2001, 57 (27) pp. 5885-5895, Bioorganic and Medicinal Chemistry Letters, 2000, 10(8), pp. 835-838 and Synthesis 2000 (1), pp. 103-108.

The reaction customarily takes place in an inert solvent, for example in an ether, such as diethyl ether, diisopropyl ether, methyl tert-butyl ether or tetrahydrofuran, a halohydrocarbon, such as dichloromethane, an aliphatic or cycloaliphatic hydrocarbon, such as pentane, hexane or cyclohexane, or an aromatic hydrocarbon, such as toluene, xylene, cumene and the like, or in a mixture of the abovementioned solvents.

The reaction of II with III is customarily carried out in the presence of an auxiliary base. Suitable bases are inorganic bases, such as sodiumcarbonate or potassiumcarbonate, or sodiumhydrogencarbonate or potassiumhydrogencarbonate, and organic bases, for example trialkylamines, such as triethylamine, or pyridine compounds, such as pyridine, lutidine and the like. The latter compounds can at the same time serve as solvents. The auxiliary base is customarily employed in at least equimolar quantities, based on the amine compound II.

The compounds of the general formula II are known per se or can be prepared in the manner shown in scheme 2.

Scheme 2:



In scheme 2, n, R^2 and Q have the previously mentioned meanings. $R^{1'}$ has the meanings different from hydrogen which are specified for R^1 or is a suitable protecting group. Suitable protecting groups are disclosed, for example, in P. Kocienski, Protecting Groups, Thieme-Verlag, Stuttgart 2000, Chapter 6. Y is a nucleophilically displaceable leaving group, in particular a halogen atom, e.g. chlorine or bromine, or an alkylsulfonyl group, e.g. methylsulfonyl.

The reaction depicted in step a) in scheme 2 takes place under the reaction conditions which are customary for a nucleophilic substitution on an aromatic radical and which are described, for example, in Tetrahedron 1999, 55(33), pp. 10243-10252, J. Med. Chem. 1997, 40(22), pp. 3679-3686 and Synthetic Communications, 1993, 23(5), pp. 591-599. Where appropriate, it can be advantageous to convert a ring nitrogen atom in the Q group into its N-oxide (see, for example, Angew. Chem. Int. Ed. Engl.,2002 41(11), pp. 1937-1940, J. Med. Chem. 1985, 28(2), pp. 248-252 and Tetrahedron Lett. 2002 43(17) pp. 3121-3123). This approach has proved to be of value, in particular, for preparing compounds I in which Q is a pyridin-2,4-diyl group. In connection with the subsequent reduction of the nitro group in VI (step b), the N-oxide group is also reduced. For this, the reduction is carried out, for example, in the presence of indium salts.

If 5-bromonitropyridine is used as compound V in step a) in accordance with scheme 2, the coupling is also achieved under palladium catalysis in the presence of an auxiliary base, for example an alkali metal carbonate such as cesium carbonate. Particularly suitable palladium catalysts in this connection are palladium(0) compounds or palladium compounds which are able to form a palladium(0) compound under reaction conditions, e.g. palladium dichloride, tetrakis(triphenylphosphine)palladium(0), tris(dibenzylideneacetone)dipalladium(0), advantageously in combination with phosphine ligands, e.g. triarylphosphines, such as triphenylphosphine,

trialkylphosphines, such as tributylphosphine, and cycloalkylphosphines, such as tricyclohexylphosphine, and, especially, using phosphine chelate ligands, such as 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl. The conditions which are required for reactions of this nature are described, for example, in Tetrahedron Lett. 2001, 42(22), p. 3681 and Tetrahedron Lett. 2002, 43(12), pp. 2171-2173.

In step b), the nitro group in VI is reduced to the NH_2 group in II. Subsequently, in step c), the NH_2 group can be converted into a $-NR^{3'}H$ group, in which $R^{3'}$ has the meanings different from hydrogen which are specified for R^3.

The reaction conditions which are required for step b) correspond to the customary conditions for reducing aromatic nitro groups which have been described extensively in the literature (see, for example, J. March, Advanced Organic Chemistry, 3rd ed., J. Wiley & Sons, New-York, 1985, p. 1183 and the literature cited in this reference).

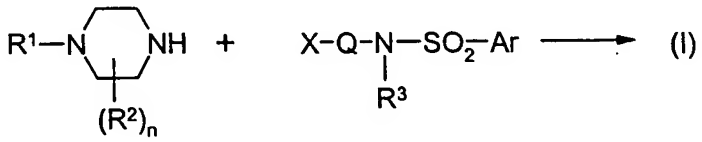
The reduction is achieved, for example, by reacting the nitro compound VII with a metal such as iron, zinc or tin under acidic reaction conditions, i.e. using nascent hydrogen, or using a complex hydride such as lithium aluminum hydride or sodium borohydride, preferably in the presence of transition metal compounds of nickel or cobalt such as $NiCl_2(P(phenyl)_3)_2$, or $CoCl_2$,(see Ono et al. Chem. Ind. (London), 1983 p.480), or using $NaBH_2S_3$ (see Lalancette et al. Can. J. Chem. 49, 1971, p. 2990), with it being possible to carry out these reductions, depending on the given reagent, in substance or in a solvent or diluent. Alternatively, the reduction of VI to II can be carried out with hydrogen in the presence of a transition metal catalyst, e.g. using hydrogen in the presence of catalysts based on platinum, palladium, nickel, ruthenium or rhodium. The catalysts can contain the transition metal in elemental form or in the form of a complex compound, of a salt or of an oxide of the transition metal, with it being possible, for the purpose of modifying the activity, to use customary coligands, e.g. organic phosphine compounds, such as triphenylphosphine, tricyclohexylphosphine or tri-n-butylphosphines or phosphites. The catalyst is customarily employed in quantities of from 0.001 to 1 mol per mol of compound VI, calculated as catalyst metal. In a preferred variant, the reduction is effected using tin(II) chloride in analogy with the methods described in Bioorganic and Medicinal Chemistry Letters, 2002, 12(15), pp. 1917-1919 and J. Med. Chem. 2002, 45(21), pp. 4679-4688. The reaction of VI with tin(II) chloride is preferably carried out in an inert organic solvent, preferably an alcohol such as methanol, ethanol, isopropanol or butanol.

Reducing VI results in compounds II in which R^3 is hydrogen. Customary methods can then be used to react these compounds with an alkylating agent $R^{3'}$-X, in which $R^{3'}$ is C_1-C_4-alkyl and X is a nucleophilically displaceable leaving group (e.g. halogen, such

as chlorine, bromine or iodine), resulting in a compound II in which R^3 = alkyl (step c). The reaction conditions which are required for this are disclosed, for example, in WO 02/83652, Tetrahedron 2000, 56(38) pp. 7553-7560 and Synlett. 2000 (4), pp. 475-480.

The compound I can also be prepared by the route depicted in scheme 3:

Scheme 3:

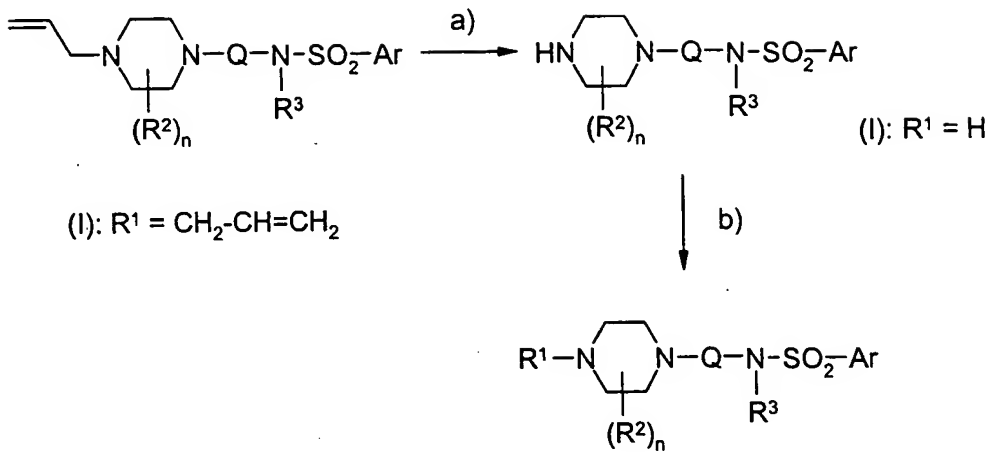


(VII) (VIII)

In scheme 3, n, R^1, R^2, R^3, Ar and Q have the previously mentioned meanings. Y is a nucleophilically displaceable leaving group, in particular a halogen atom, e.g. chlorine or bromine, or an alkylsulfonyl group, e.g. methylsulfonyl. The reaction of VII with VIII, as depicted in scheme 3, takes place under the reaction conditions specified for scheme 2, step a). Compounds of the general formula I are known or can be prepared in analogy with the methods known from the literature.

Compounds of general formula I, in which R is an allyl group, can be converted into compounds possessing different R^1 substituents using the route shown in scheme 4.

Scheme 4:



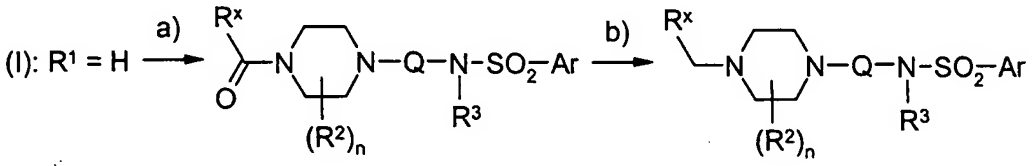
In scheme 4, n, R^2, R^3, Ar and Q have the previously mentioned meaning. The elimination of the allyl group, as depicted in step a) in scheme 4, is achieved, for example, by reacting I [R^1 = allyl] with an allyl trapping agent, such as mercaptobenzoic acid or 1,3-dimethylbarbituric acid, in the presence of catalytic quantities of palladium (0) compounds or palladium compounds which are able to form a palladium(0) compound under reaction conditions, e.g. palladium dichloride, tetrakis(triphenylphosphine)palladium(0) or tris(dibenzylideneacetone)dipalladium(0), advantageously in combination with phosphine ligands, e.g. triarylphosphines, such as triphenylphosphine, trialkylphosphines, such as tributylphosphine, and cycloalkylphosphines, such as tricyclohexylphosphine, and especially with phosphine chelate ligands, such as 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl or 1,4-bis(diphenylphosphino)butane, using methods known from the literature (with regard to eliminating N-allyl in the presence of mercaptobenzoic acid, see WO 94/24088; with regard to eliminating in the presence of 1,3-dimethylbarbituric acid, see J. Am. Chem. Soc. 2001, 123 (28), pp. 6801-6808 and J. Org. Chem 2002, 67(11) pp. 3718-3723). Alternatively, the elimination of N-allyl, as depicted in scheme 4 step a), can also be effected by reacting in the presence of rhodium compounds, such as tris(triphenylphosphine)chlororhodium(I), using methods known from the literature (see J. Chem. Soc., Perkin Transaction I: Organic and Bio-Organic Chemistry 1999 (21) pp. 3089-3104 and Tetrahedron Asymmetry 1997, 8(20), pp. 3387 - 3391).

The resulting piperazine compound I [R^1 = H] can then be reacted, in a known manner, in the sense of an alkylation, with a compound R^1-X. In this compound, R^1 is C_1-C_4-alkyl, C_3-C_6-cycloalkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl or C_3-C_6-cycloalkyl-C_1-C_4-alkyl and X is a nucleophilically displaceable leaving group, e.g. halogen, trifluoroacetate, alkylsulfonate, arylsulfonate, alkyl sulfate and the like. The reaction conditions which are required for the alkylation in step b) have been adequately disclosed, e.g. in Bioorganic and Medicinal Chemistry Lett. 2002, 12(7), pp. 2443-2446 and also 2002, 12(5), pp. 1917-1919.

The conversion, as depicted in scheme 4, step b), of the piperazine compound I [R^1 = H] obtained in step a) can also be achieved, in the sense of a reductive amination, by reacting I [R^1 = H] with a suitable ketone or aldehyde in the presence of a reducing agent, e.g. in the presence of a borohydride such as sodium borohydride, sodium cyanoborohydride or sodium triacetoxyborohydride. The skilled person is familiar with the reaction conditions which are required for a reductive amination, e.g. from Bioorganic and Medicinal Chemistry Lett. 2002, 12(5), pp. 795-798 and 12(7) pp. 1269-1273.

The conversion, as depicted in scheme 4, step b), of the piperazine compound I [R^1 = H] obtained in step a) can also be achieved by successive acylation and subsequent reduction of the acylation product, using the method depicted in scheme 4a:

Scheme 4a:



R^x = alkyl, cycloalkyl,
cycloalkylalkyl, alkenyl
haloalkyl, alkynyl
alkoxyalkyl, hydroxyalkyl

In scheme 4a, n, R^2, R^3, Ar and Q have the previously mentioned meanings. The acylation in step a) and the reduction in step b) are effected using standard methods of organic chemistry as are described, for example, in J. March, Advanced Organic Chemistry, 3rd ed. J. Wiley & Sons, New York 1985, p.370 and 373 (acylation) and p. 1099 f. and in the literature cited in this publication (with regard to acylation, see also

Synth. Commun. 1986, 16, p. 267, and with regard to reduction, see also J. Heterocycl. Chem. 1979, 16, p. 1525).

In compounds of the general formula I which carry a halogen atom, in particular bromine or iodine, on the aromatic radical Ar, the halogen atom can be converted into an alkyl, alkenyl, cycloalkyl, alkynyl or cycloalkylalkyl group using methods which are known per se. The conversion is achieved by coupling the halo compound I to an alkyl-, alkenyl-, alkynyl-, cycloalkyl- or cycloalkylalkyl-boronic acid compound under the conditions of a Suzuki coupling as is described, for example, in Tetrahedron Lett. 2002, 43, pp. 6987-6990; Chem. Rev. 1995, 95, pp. 2457-2483 and J. Org. Chem. 66(21) (2001), pp. 7124-7128.

If not otherwise indicated, the above-described reactions are generally carried out in a solvent at temperatures between room temperature and the boiling temperature of the solvent employed. Alternatively, the activation energy which is required for the reaction can be introduced into the reaction mixture using microwaves, something which has proved to be of value, in particular, in the case of the reactions catalyzed by transition metals (with regard to reactions using microwaves, see Tetrahedron 2001, 57, p. 9199 ff. p. 9225 ff. and also, in a general manner, "Microwaves in Organic Synthesis", André Loupy (Ed.), Wiley-VCH 2002.

Examples of solvents which can be used are ethers, such as diethyl ether, diisopropyl ether, methyl tert-butyl ether or tetrahydrofuran, aprotic polar solvent, such as dimethylformamide, dimethyl sulfoxide, dimethoxyethane, and acetonitrile, aromatic hydrocarbons, such as toluene and xylene, ketones, such as acetone or methyl ethyl ketone, halohydrocarbons, such as dichloromethane, trichloromethane and dichloroethane, esters, such as ethyl acetate and methyl butyrate, carboxylic acids, such as acetic acid or propionic acid, and alcohols, such as methanol, ethanol, n-propanol, isopropanol and butanol.

If desired, it is possible for a base to be present in order to neutralize protons which are released in the reactions. Suitable bases include inorganic bases, such as sodium carbonate, potassium carbonate, sodium hydrogen carbonate or potassium hydrogen carbonate, and, in addition, alkoxides, such as sodium methoxide or sodium ethoxide, alkali metal hydrides, such as sodium hydride, and also organometallic compounds, such as butyllithium compounds or alkylmagnesium compounds, or organic nitrogen bases, such as triethylamine or pyridine. The latter compounds can at the same time serve as solvents.

The crude product is isolated in a customary manner, for example by filtering, distilling off the solvent or extracting from the reaction mixture, etc. The resulting compounds can be purified in a customary manner, for example by means of recrystallizing from a solvent, by means of chromatography or by means of converting into an acid addition salt.

The acid addition salts are prepared in a customary manner by mixing the free base with a corresponding acid, where appropriate in solution in an organic solvent, for example a lower alcohol, such as methanol, ethanol or propanol, an ether, such as methyl tert-butyl ether or diisopropyl ether, a ketone, such as acetone or methyl ethyl ketone, or an ester, such as ethyl acetate.

The compounds according to the invention of the formula I are highly selective dopamine D_3 receptor ligands which, because of their low affinity for other receptors such as D_1 receptors, D_4 receptors, α1-adrenergic and/or α2-adrenergic receptors, muscarinergic receptors, histamine receptors, opiate receptors and, in particular, dopamine D_2 receptors, give rise to fewer side-effects than do the classic neuroleptics, which are D_2 receptor antagonists.

The high affinity of the compounds according to the invention for D_3 receptors is reflected in very low in-vitro K_i values of as a rule less than 100 nM (nmol/l), in particular less than 50 nM and, in particular, of less than 10 nM. The displacement of [^{125}I]-iodosulpride can, for example, be used in receptor binding studies for determining binding affinities for D_3 receptors.

The selectivity $K_i(D_2)/K_i(D_3)$ of the compounds according to the invention is as a rule at least 10, preferably at least 30, even better at least 50 and particularly advantageously at least 100. The displacement of [^{3}H]SCH23390, [^{125}I] iodosulpride or [^{125}I] spiperone can be used, for example, for carrying out receptor binding studies on D_1, D_2 and D_4 receptors.

Because of their binding profile, the compounds can be used for treating diseases which respond to dopamine D_3 ligands, i.e. they are effective for treating those disturbances or diseases in which exerting an influence on (modulating) the dopamine D_3 receptors leads to an improvement in the clinical picture or to the disease being cured. Examples of these diseases are disturbances or diseases of the central nervous system.

Disturbances or diseases of the central nervous system are understood as meaning disturbances which affect the spinal chord and, in particular, the brain. Within the

meaning of the invention, the term "disturbance" denotes anomalies which are as a rule regarded as being pathological conditions or functions and which can manifest themselves in the form of particular signs, symptoms and/or malfunctions. While the treatment according to the invention can be directed toward individual disturbances, i.e. anomalies or pathological conditions, it is also possible for several anomalies, which may be causatively linked to each other, to be combined into patterns, i.e. syndromes, which can be treated in accordance with the invention.

The disturbances which can be treated in accordance with the invention are, in particular, psychiatric and neurological disturbances. These disturbances include, in particular, organic disturbances, including symptomatic disturbances, such as psychoses of the acute exogenous reaction type or attendant psychoses of organic or exogenous cause, e.g., in association with metabolic disturbances, infections and endocrinopathogies; endogenous psychoses, such as schizophrenia and schizotype and delusional disturbances; affective disturbances, such as depressions, mania and/or manic-depressive conditions; and also mixed forms of the above-described disturbances; neurotic and somatoform disturbances and also disturbances in association with stress; dissociative disturbances, e.g. loss of consciousness, clouding of consciousness, double consciousness and personality disturbances; disturbances in attention and waking/sleeping behavior, such as behavioral disturbances and emotional disturbances whose onset lies in childhood and youth, e.g. hyperactivity in children, intellectual deficits, in particular attention disturbances (attention deficit disorders), memory disturbances and cognitive disturbances, e.g. impaired learning and memory (impaired cognitive function), dementia, narcolepsy and sleep disturbances, e.g. restless legs syndrome; development disturbances; anxiety states, delirium; sexlife disturbances, e.g. impotence in men; eating disturbances, e.g. anorexia or bulimia; addiction; and other unspecified psychiatric disturbances.

The disturbances which can be treated in accordance with the invention also include Parkinson's disease and epilepsy and, in particular, the affective disturbances connected thereto.

The addiction diseases include psychic disturbances and behavioral disturbances which are caused by the abuse of psychotropic substances, such as pharmaceuticals or narcotics, and also other addiction diseases, such as addiction to gaming (impulse control disorders not elsewhere classified). Examples of addictive substances are: opioids (e.g. morphine, heroin and codeine), cocaine; nicotine; alcohol; substances which interact with the GABA chloride channel complex, sedatives, hypnotics and tranquilizers, for example benzodiazepines; LSD; cannabinoids; psychomotor stimulants, such as 3,4-methylenedioxy-N-methylamphetamine (ecstasy);

amphetamine and amphetamine-like substances such as methylphenidate and other stimulants including caffeine. Addictive substances which come particularly into consideration are opioids, cocaine, amphetamine or amphetamine-like substances, nicotine and alcohol.

With regard to the treatment of addiction diseases, particular preference is given to those compounds according to the invention of the formula I which themselves do not possess any psychotropic effect. This can also be observed in a test using rats, which, after having been administered compounds which can be used in accordance with the invention, reduce their self administration of psychotropic substances, for example cocaine.

According to another aspect of the present invention, the compounds according to the invention are suitable for treating disturbances whose causes can at least partially be attributed to an anomalous activity of dopamine D_3 receptors.

According to another aspect of the present invention, the treatment is directed, in particular, toward those disturbances which can be influenced, within the sense of an expedient medicinal treatment, by the binding of preferably exogeneously administered binding partners (ligands) to dopamine D_3 receptors.

The diseases which can be treated with the compounds according to the invention are frequently characterized by progressive development, i.e. the above-described conditions change over the course of time; as a rule, the severity increases and conditions may possibly merge into each other or other conditions may appear in addition to those which already exist.

The compounds according to the invention can be used to treat a large number of signs, symptoms and/or malfunctions which are connected with the disturbances of the central nervous system and, in particular, the abovementioned conditions. These signs, symptoms and/or malfunctions include, for example, a disturbed relationship to reality, lack of insight and ability to meet customary social norms or the demands made by life, changes in temperament, changes in individual drives, such as hunger, sleep, thirst, etc., and in mood, disturbances in the ability to observe and combine, changes in personality, in particular emotional lability, hallucinations, ego-disturbances, distractedness, ambivalence, autism, depersonalization and false perceptions, delusional ideas, chanting speech, lack of synkinesia, short-step gait, flexed posture of trunk and limbs, tremor, poverty of facial expression, monotonous speech, depressions, apathy, impeded spontaneity and decisiveness, impoverished association ability, anxiety, nervous agitation, stammering, social phobia, panic disturbances,

withdrawal symptoms in association with dependency, maniform syndromes, states of excitation and confusion, dysphoria, dyskinetic syndromes and tic disturbances, e.g. Huntington's chorea and Gilles-de-la-Tourette's syndrome, vertigo syndromes, e.g. peripheral positional, rotational and oscillatory vertigo, melancholia, hysteria, hypochondria and the like.

Within the meaning of the invention, a treatment also includes a preventive treatment (prophylaxis), in particular as relapse prophylaxis or phase prophylaxis, as well as the treatment of acute or chronic signs, symptoms and/or malfunctions. The treatment can be orientated symptomatically, for example as the suppression of symptoms. It can be effected over a short period, be orientated over the medium term or can be a long-term treatment, for example within the context of a maintenance therapy.

The compounds according to the invention are preferentially suitable for treating diseases of the central nervous system, in particular for treating affective disturbances; neurotic disturbances, stress disturbances and somatoform disturbances and psychoses, and, in particular, for treating schizophrenia and depression. Because of their high selectivity with regard to the D_3 receptor, the compounds I according to the invention are also suitable for treating disturbances of kidney function, in particular disturbances of kidney function which are caused by diabetes mellitus (see WO 00/67847) and, especially, diabetic nephropathy.

Within the context of the treatment, the use according to the invention of the described compounds involves a method. In this method, an effective quantity of one or more compounds, as a rule formulated in accordance with pharmaceutical and veterinary practice, is administered to the individual to be treated, preferably a mammal, in particular a human being, productive animal or domestic animal. Whether such a treatment is indicated, and in which form it is to take place, depends on the individual case and is subject to medical assessment (diagnosis) which takes into consideration signs, symptoms and/or malfunctions which are present, the risks of developing particular signs, symptoms and/or malfunctions, and other factors.

As a rule, the treatment is effected by means of single or repeated daily administration, where appropriate together, or alternating, with other active compounds or active compound-containing preparations such that a daily dose of preferably from about 0.1 to 1000 mg/kg of bodyweight, in the case of oral administration, or of from about 0.1 to 100 mg/kg of bodyweight, in the case of parenteral administration, is supplied to an individual to be treated.

The invention also relates to the production of pharmaceutical compositions for treating an individual, preferably a mammal, in particular a human being, productive animal or domestic animal. Thus, the ligands are customarily administered in the form of pharmaceutical compositions which comprise a pharmaceutically acceptable excipient together with at least one ligand according to the invention and, where appropriate, other active compounds. These compositions can, for example, be administered orally, rectally, transdermally, subcutaneously, intravenously, intramuscularly or intranasally.

Examples of suitable pharmaceutical formulations are solid medicinal forms, such as powders, granules, tablets, in particular film tablets, lozenges, sachets, cachets, sugar-coated tablets, capsules, such as hard gelatin capsules and soft gelatin capsules, suppositories or vaginal medicinal forms, semisolid medicinal forms, such as ointments, creams, hydrogels, pastes or plasters, and also liquid medicinal forms, such as solutions, emulsions, in particular oil-in-water emulsions, suspensions, for example lotions, injection preparations and infusion preparations, and eyedrops and eardrops. Implanted release devices can also be used for administering inhibitors according to the invention. In addition, it is also possible to use liposomes or microspheres. When producing the compositions, inhibitors according to the invention are usually mixed or diluted with an excipient. Excipients can be solid, semisolid or liquid materials which serve as vehicles, carriers or medium for the active compound.

Suitable excipients are listed in the specialist medicinal monographs. In addition, the formulations can comprise pharmaceutically acceptable carriers or customary auxiliary substances, such as glidants; wetting agents; emulsifying and suspending agents; preservatives; antioxidants; antiirritants; chelating agents; coating auxiliaries; emulsion stabilizers; film formers; gel formers; odor masking agents; taste corrigents; resin; hydrocolloids; solvents; solubilizers; neutralizing agents; diffusion accelerators; pigments; quaternary ammonium compounds; refatting and overfatting agents; raw materials for ointments, creams or oils; silicone derivatives; spreading auxiliaries; stabilizers; sterilants; suppository bases; tablet auxiliaries, such as binders, fillers, glidants, disintegrants or coatings; propellants; drying agents; opacifiers; thickeners; waxes; plasticizers and white mineral oils. A formulation in this regard is based on specialist knowledge as described, for example, in Fiedler, H.P., Lexikon der Hilfsstoffe für Pharmazie, Kosmetik und angrenzende Gebiete [Encyclopedia of auxiliary substances for pharmacy, cosmetics and related fields], 4th edition, Aulendorf: ECV-Editio-Kantor-Verlag, 1996.

The following examples serve to explain the invention without limiting it.

The magnetic nuclear resonance spectral properties (NMR) refer to the chemical shifts (δ) expressed in parts per million (ppm). The relative area of the shifts in the ^{1}H NMR spectrum corresponds to the number of hydrogen atoms for a particular functional type in the molecule. The nature of the shift, as regards multiplicity, is indicated as singlet (s), broad singlet (s. br.), doublet (d), broad doublet (d br.), triplet (t), broad triplet (t br.), quartet (q), quintet (quint.) and multiplet (m).

Preparation Examples

Example 1: N-[6-(4-Allylpiperazin-1-yl)pyridin-3-yl]-4-isopropylbenzenesulfonamide

1.1 1-Allyl-4-(5-nitropyridin-2-yl)piperazine

2.0 g (12.61 mmol) of 2-chloro-5-nitropyridine were dissolved in 8 ml of dimethylformamide, and 3.49 g (25.23 mmol) of potassium carbonate were added. After that, a solution of 1.75 g (13.88 mmol) of N-allylpiperazine in 2 ml of dimethylformamide was added slowly dropwise to the reaction mixture (exothermic reaction). The reaction mixture was then stirred at room temperature for 2 hours. After the solvent had been concentrated down to dryness, the resulting residue was stirred up in 100 ml of heptane. The precipitate which remained was filtered off with suction. The filtrate was concentrated, resulting in 720 mg of the title compound. The precipitate which had been filtered off with suction was treated with 150 ml of water and extracted three times with diethyl ether. The organic phase was washed with a saturated solution of sodium chloride and dried over sodium sulfate. A further 2.24 g of the title compound were isolated after the solvent had been filtered and concentrated down to dryness. The total yield of 1-allyl-4-(5-nitropyridin-2-yl)piperazine was 2.96 g (95% of theory).

MS [m+1]: 249.

1.2 6-(4-Allylpiperazin-1-yl)pyridine-3-amine

2.2 g (8.86 mmol) of 1-allyl-4-(5-nitropyridin-2-yl)piperazine from Example 1.1 were dissolved in 150 ml of methanol after which 18 g (79.75 mmol) of tin(II) chloride dihydrate were added and the mixture was stirred at 70 °C for 4 hours. After the solvent had been evaporated down to dryness, water was added to the residue. The aqueous reaction mixture was made alkaline with dilute sodium hydroxide solution and then extracted with ethyl acetate. The solid which had precipitated out was filtered off. After that, the phases were separated and the aqueous phase was extracted in each case twice with ethyl acetate and dichloromethane. The combined organic phases were dried over sodium sulfate.

1.74 g (90% of theory) of the title compound were obtained after the drying agent had been removed and the solvent had been evaporated down to dryness.

MS [m+1]: 219.

1.3 N-[6-(4-Allylpiperazin-1-yl)pyridin-3-yl]-4-isopropylbenzenesulfonamide

1.4 g (7.97 mmol) of 6-(4-allylpiperazin-1-yl)pyridin-3-ylamine from Example 1.2 and 1.74 g (7.97 mmol) of 4-isopropylbenzenesulfonyl chloride were dissolved in 30 ml of tetrahydrofuran at room temperature. 3.3 ml (23.91 mmol) of triethylamine were then added to this mixture. After that, the reaction mixture was stirred overnight at room temperature. After the solvent had been evaporated to dryness, water was added to the residue. The aqueous reaction mixture was made acid with 1N hydrochloric acid and extracted twice with diethyl ether. After that, the aqueous phase was made alkaline (pH 9-10) with a 1N aqueous solution of sodium hydroxide and then extracted twice with diethyl ether. After the combined organic phases had been dried over sodium sulfate, the drying agent had been filtered off and the solvent had been evaporated down to dryness, the resulting residue was chromatographed on silica gel using cyclohexane/ethyl acetate (45:55% to 100% ethyl acetate). The filtrate was evaporated down to dryness. The resulting residue was thoroughly stirred in 10 ml of heptane, filtered off in suction and dried, with 1.93 g (61% of theory) of the title compound being obtained.

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] 7.7 (s, 1H); 7.6 (d, 2H); 7.4 (d, 1H); 7.3 (d, 2H); 6.6 (d, 1H); 6.4 (bs, 1H); 5.9 (m, 1H); 5.2 (m, 2H); 3.5 (m, 4H); 3.1 (m, 2H); 3.0 (m, 1H); 2.5 (m, 4H); 1.2 (d, 6H).

MS [m+1]: 401.

Example 2: N-[6-(4-Allylpiperazin-1-yl)pyridin-3-yl]-4-propylbenzenesulfonamide

373 mg of the title compound were obtained in an analogous manner to that described in Example 1.3 when starting with 4-n-propylbenzenesulfonyl chloride.

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] 7.7 (m, 1H); 7.6 (m, 2H); 7.4 (d, 1H); 7.3 (m, 2H); 6.6 (d, 1H); 6.3 (bs, 1H); 5.9 (m, 1H); 5.2 (m, 2H); 3.5 (m, 4H); 3.1 (m, 2H); 2.6 (m, 2H); 2.5 (m, 4H); 1.7 (m, 2H); 0.9 (m, 3H).

MS [m+1]: 401.

Example 3: N-[6-(4-Allylpiperazin-1-yl)pyridin-3-yl]-4-butylbenzenesulfonamide

405 mg of the title compound were obtained in an analogous manner to that described in Example 1.3 when starting with 4-n-butylbenzenesulfonyl chloride.

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] 7.7 (m, 1H); 7.6 (m, 2H); 7.4 (d, 1H); 7.3 (m, 2H); 6.6 (d, 1H); 6.2 (bs, 1H); 5.9 (m, 1H); 5.2 (m, 2H); 3.5 (m, 4H); 3.0 (m, 2H); 2.7 (m, 2H); 2.5 (m, 4H); 1.6 (m, 2H); 1.4 (m, 2H); 0.9 (m, 3H).

MS [m+1]: 415.

Example 4: N-[6-(4-Allylpiperazin-1-yl)pyridin-3-yl]-4-trifluoromethylbenzenesulfonamide

500 mg of the title compound were obtained in an analogous manner to that described in Example 1.3 when starting with 4-trifluoromethylbenzenesulfonyl chloride.

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] 7.9 (d, 2H); 7.8 (m, 3H); 7.3 (d, 1H); 6.6 (d, 1H); 5.9 (m, 1H); 5.2 (m, 2H); 3.5 (m, 4H); 3.1 (m, 2H); 2.5 (m, 4H).

MS [m+1]: 427.

Example 5: N-[6-(4-Allylpiperazin-1-yl)pyridin-3-yl]-4-ethylbenzenesulfonamide hydrochloride

The Example 1.3 was repeated with 4-ethylbenzenesulfonyl chloride being used instead of 4-isopropylbenzenesulfonyl chloride. The resulting reaction product was converted into the hydrochloride with ethereal hydrochloric acid, with 480 mg (please complete) of the title compound being obtained.

^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] 11.5 (bs, 1H); 10.0 (s, 1H); 7.8 (d, 2H); 7.6 (d, 2H); 7.4 (m, 3H); 6.9 (d, 1H); 6.0 (m, 1H); 5.5 (m, 2H); 4.3 (m, 2H); 3.8 (m, 2H); 3.4 (m, 2H); 3.3 (m, 2H); 3.0 (m, 2H); 2.7 (m, 2H); 1.2 (t, 3H).

MS [m+1]: 387 (free base).

Example 6: N-[6-(4-Allylpiperazin-1-yl)pyridin-3-yl]-4-vinylbenzenesulfonamide hydrochloride

Example 1.3 was repeated with 4-vinylbenzenesulfonyl chloride being used instead of 4-isopropylbenzenesulfonyl chloride. The resulting reaction product was converted into the hydrochloride with ethereal hydrochloric acid, with 300 mg of the title compound being obtained.

^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] 11.1 (bs, 1H); 10.0 (s, 1H); 7.8 (d, 1H); 7.6 (m, 4H); 7.3 (d, 1H); 6.9 (d, 1H); 6.8 (dd, 1H); 6.0 (m, 2H); 5.5 (m, 3H); 4.3 (m, 2H); 3.8 (m, 2H); 3.4 (m, 2H); 3.2 (m, 2H); 3.0 (m, 2H).

MS [m+1]: 385 (free base).

Example 7: 4-Isopropyl-N-(6-piperazin-1-ylpyridin-3-yl)benzenesulfonamide

95 mg (0.1 mmol) of tris-(dibenzylideneacetone)dipalladium(0) and 44 mg (0.1 mmol) of 1,4-bis-(diphenylphosphino)butane were dissolved in 10 ml of tetrahydrofuran under an argon atmosphere. A solution composed of 1.1 g (2.75 mmol) of N-[6-(4-allylpiperazin-1-yl)pyridin-3-yl]-4-isopropylbenzenesulfonamide from Example 1.3 l in 3 ml of tetrahydrofuran was then added dropwise to the reaction mixture. After that, a solution of 386 mg (2.5 mmol) of 2-mercaptobenzoic acid in 2 ml of tetrahydrofuran was added dropwise to the reaction mixture and the mixture was stirred at room temperature for 90 minutes. A solution of a further 386 mg (2.5 mmol) of 2-mercaptobenzoic acid in 2 ml of tetrahydrofuran was then added dropwise to the reaction mixture. The reaction mixture was stirred overnight at room temperature and, after that, the solvent was evaporated down to dryness. 150 ml of water were added to the resulting residue, after which the mixture was made acid with 1N aqueous hydrochloric acid and extracted three times with diethyl ether. The aqueous phase was then made alkaline, to pH > 11, with a 1N aqueous solution of sodium hydroxide and subsequently extracted three times with dichloromethane. After that, the aqueous phase was adjusted to pH 8-9, saturated with an aqueous solution of sodium chloride and, after that, extracted several times with dichloromethane. 840 mg (82% of theory) of the title compound were obtained after the combined organic phases had been dried over sodium sulfate and the solvent had been filtered and evaporated down to dryness.

^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] 7.7 (d, 1H); 7.6 (d, 2H); 7.4 (dd, 1H); 7.3 (d, 2H); 6.6 (d, 1H); 3.5 (m, 4H); 3.0 (m, 5H); 1.2 (d, 6H).

MS [m+1]: 361.

Example 8: N-{6-[4-(Cyclohexylmethyl)piperazin-1-yl]pyridin-3-yl}-4-isopropyl-benzenesulfonamide hydrochloride

150 mg (0.42 mmol) of 4-isopropyl-N-(6-piperazin-1-yl-pyridin-3-yl)-benzenesulfonamide from Example 7 and 51 mg (0.46 mmol) of cyclohexanealdehyde were dissolved in 5 ml of dichloromethane and 40 µl (0.62 mmol) of glacial acetic acid under a nitrogen atmosphere. 133 mg

(0.63 mmol) of sodium trisacetoxyborohydride were then added. The mixture was stirred at room temperature for 90 minutes and, after that, the solvent was evaporated down to dryness. The resulting residue was taken up in water and this mixture was made to pH > 11 with a 1N aqueous solution of sodium hydroxide. After that, the aqueous reaction mixture was extracted with diethyl ether. After the organic phase had been dried over sodium sulfate and the solvent had been filtered and evaporated down to dryness, the resulting residue was converted into the hydrochloride with ethereal hydrochloric acid, resulting in 156 mg (76% of theory) of the title compound.

^{1}H-NMR (500 MHz, DMSO-d_6): δ [ppm] 10.4 (bs, 1H); 10.0 (s, 1H); 7.8 (d, 1H); 7.6 (d, 2H); 7.4 (d, 2H); 7.3 (d, 1H); 6.9 (d, 1H); 4.2 (m, 2H); 3.5 (m, 2H); 3.4 (m, 2H); 3.0 (m, 5H); 1.8 (m, 3H); 1.7 (m, 3H); 1.2 (m, 9H); 1.0 (m, 2H).

MS [m+1]: 457 (free base).

The compounds of Examples 9 to 12 were prepared in an analogous manner.

Example 9: N-[6-(4-Isobutylpiperazin-1-yl)pyridin-3-yl]-4-isopropylbenzenesulfonamide hydrochloride

^{1}H-NMR (500 MHz, DMSO-d_6): δ [ppm] 10.4 (bs, 1H); 10.0 (s, 1H); 7.8 (m, 1H); 7.6 (d, 2H); 7.5 (d, 2H); 7.4 (m, 1H); 6.9 (d, 1H); 4.2 (d, 2H); 3.5 (d, 2H); 3.4 (m, 2H); 3.0 (m, 5H); 2.1 (m, 1H); 1.2 (d, 6H); 1.0 (d, 6H).

MS [m+1]: 417 (free base).

Example 10: 4-Isopropyl-N-[6-(4-methylpiperazin-1-yl)pyridin-3-yl]benzenesulfonamide

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] 7.7 (d, 1H); 7.6 (d, 2H); 7.4 (dd, 1H); 7.3 (d, 2H); 6.6 (d, 1H); 3.5 (m, 4H); 3.0 (m, 1H); 2.5 (m, 4H); 2.3 (s, 3H); 1.2 (d, 6H).

MS [m+1]: 375.

Example 11: N-[6-(4-Ethylpiperazin-1-yl)pyridin-3-yl]-4-isopropylbenzenesulfonamide hydrochloride

^{1}H-NMR (500 MHz, DMSO-d_6): δ [ppm] 10.4 (bs, 1H); 10.0 (s, 1H); 7.8 (d, 1H); 7.6 (d, 2H); 7.4 (d, 2H); 7.3 (d, 1H); 6.9 (d, 1H); 4.3 (m, 2H); 3.5 (m, 2H); 3.2 (m, 2H); 3.1 (m, 2H); 3.0 (m, 3H); 1.3 (m, 3H); 1.2 (d, 6H).

MS [m+1]: 389 (free base).

Example 12: N-{6-[4-(Cyclopropylmethyl)piperazin-1-yl]pyridin-3-yl}-4-isopropylbenzenesulfonamide hydrochloride

^{1}H-NMR (500 MHz, DMSO-d_6): δ [ppm] 10.8 (bs, 1H); 10.0 (s, 1H); 7.8 (d, 1H); 7.6 (d, 2H); 7.4 (d, 2H); 7.3 (d, 1H); 6.9 (d, 1H); 4.3 (m, 2H); 3.6 (m, 2H); 3.3 (m, 2H); 3.0 (m, 5H); 1.2 (d, 6H); 1.1 (m, 1H); 0.6 (m, 2H); 0.4 (m, 2H).

MS [m+1]: 415 (free base)

Example 13: N-[6-(4-Allyl-3-methylpiperazin-1-yl)pyridin-3-yl]-4-isopropylbenzenesulfonamide hydrochloride

13.1 3-Methyl-1-(5-nitropyridin-2-yl)piperazine

872 mg (6.31 mmol) of potassium carbonate were added to a solution of 500 mg (3.15 mmol) of 2-chloro-5-nitropyridine in 7 ml of dimethylformamide. After that, a solution of 350 mg (3.32 mmol) of 2-methylpiperazine in 3 ml of dimethylformamide was slowly added dropwise to the reaction mixture while cooling with ice (exothermic reaction). The reaction mixture was stirred for 1 hour while cooling with ice and then stirred overnight at room temperature. After the solvent had been evaporated to dryness, the residue was taken up in water and this mixture was extracted three times with diethyl ether. The combined organic phases were dried over sodium sulfate, filtered and evaporated to dryness, with 3-methyl-1-(5-nitropyridin-2-yl)piperazine (Yield: 650 mg, 89% of theory) being obtained.

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] 9.0 (s, 1H); 8.2 (d, 1H); 6.6 (d, 1H), 4.4 (m, 2H); 3.2 (m, 1H); 3.1 (m, 1H); 2.9 (m, 2H); 2.7 (m, 1H); 1.2 (m, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): 160.4 (C); 146.5 (CH); 134.9 (C); 133.0 (C); 104.5 (CH); 52.2 (CH_2); 50.6 (CH); 45.7 (CH_2); 45.4 (CH_2); 19.6 (CH_3).

13.2 1-Allyl-2-methyl-4-(5-nitropyridin-2-yl)piperazine

630 mg (2.72 mmol) of 3-methyl-1-(5-nitropyridin-2-yl)piperazine from Example 13.1 and 267 µl (3.09 mmol) of allyl bromide were dissolved in 10 ml of dimethylformamide. 1.2 ml (8.4 mmol) of triethylamine were then added dropwise to the solution. After the mixture had been stirred at room temperature for 1 hour, a further 65 µl (0.75 mmol) of allyl bromide were added dropwise to the reaction mixture, which was then stirred for a further hour. After that, a further 65 µl (0.75 mmol) of allyl bromide and 0.5 ml (3.6 mmol) of triethylamine were added dropwise. The mixture was then stirred overnight at room temperature. After the solvent had been evaporated down to dryness, the resulting residue was taken up in water and this solution was made alkaline using a 1N aqueous solution of

sodium hydroxide. After that, the aqueous reaction mixture was extracted three times with diethyl ether. The combined organic phases were dried over sodium sulfate, filtered and evaporated down to dryness, with 707 mg (90% of theory) of the title compound being obtained.

MS [m+1]: 263.

13.3 6-(4-Allyl-3-methylpiperazin-1-yl)pyridine-3-amine

4.975 g (22.05 mmol) of tin(II) chloride dihydrate were added to a solution of 707 mg (2.45 mmol) of 1-allyl-2-methyl-4-(5-nitropyridin-2-yl)piperazine from Example 13.2 in 50 ml of methanol and the resulting mixture was stirred at 70°C for 90 minutes. After the solvent had been evaporated down to dryness, water was added to the resulting residue and the mixture was made alkaline using a dilute aqueous solution of sodium hydroxide. After that, the aqueous reaction mixture was extracted with ethyl acetate. The solid which had precipitated out was filtered off with suction and the phases were separated. The aqueous phase was extracted with dichloromethane. After that, the combined organic phases were dried over sodium sulfate, filtered and evaporated down to dryness. The resulting title compound was used in the next step without any further purification.

MS [m+1]: 233.

13.4 N-[6-(4-Allyl-3-methylpiperazin-1-yl)pyridin-3-yl]-4-isopropylbenzenesulfonamide hydrochloride

305 mg (1.31 mmol) of 6-(4-allyl-3-methylpiperazin-1-yl)pyridin-3-ylamine from Example 13.3 and 301 mg (1.38 mmol) of 4-isopropylbenzenesulfonyl chloride were dissolved in 10 ml of tetrahydrofuran at room temperature, after which 0.55 ml (3.94 mmol) of triethylamine was added dropwise. After that, the reaction mixture was stirred overnight at room temperature. After the solvent had been evaporated down to dryness, the resulting residue was treated with water and the mixture was made acid with 1N hydrochloric acid and extracted twice with diethylether. The aqueous phase was made alkaline, to pH 9-10, using a 1N aqueous solution of sodium hydroxide and then extracted twice with diethyl ether. After the combined organic phases had been dried over sodium sulfate and the solvent had been filtered and evaporated down to dryness, the resulting residue was purified by column chromatography (cyclohexane/ethylacetate from 50:50 to 20:80). After that, the filtrate was evaporated down to dryness. The resulting residue was converted into the hydrochloride using ethereal hydrochloric acid, with 417 mg (74% of theory) of the title compound being obtained.

^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] 11.3 (bs, 1H); 10.0 (s, 1H); 7.8 (d, 1H); 7.6 (d, 2H); 7.4 (d, 2H); 7.3 (d, 1H); 6.9 (d,1 H); 6.0 (m, 1H); 5.5 (m, 2H); 4.3 (m,

1H); 4.0 (m, 1H); 3.7 (m, 1H); 3.4 (m, 1H); 3.2 (m, 3H); 3.0 (m, 3H); 1.4 (d, 3H); 1.2 (d, 6H).

MS [m+1]: 415 (free base).

Example 13a: N-{6-[4-Allyl-(3S)-methylpiperazin-1-yl]pyridin-3-yl}-4-isopropylbenzenesulfonamide (S enantiomer as free base)

The preparation was effected in analogy with the preparation of the racemic compound, with enantiomerically pure (2S)-methylpiperazine being used in step 13.1 instead of racemic 2-methylpiperazine.

^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] 11.3 (bs, 1H); 10.0 (s, 1H); 7.8 (s, 1H); 7.6 (d, 2H); 7.4 (d, 1H); 7.3 (d, 1H); 6.9 (d, 1H); 6.0 (m, 1H); 5.5 (m, 2H); 4.3 (m, 2H); 4.0 (m, 1H); 3.7 (m, 1H); 3.4 (m, 1H); 3.2 (m, 2H); 3.1 (m, 1H); 3.0 (m, 2H).1.4 (d, 3H); 1.2 (d, 6H).

MS [m+1]: 415 (free base)

Example 14: 4-Isopropyl-N-[6-(3-methyl-4-propylpiperazin-1-yl)pyridin-3-yl]benzenesulfonamide hydrochloride

100 mg (0.24 mmol) of N-[6-(4-allyl-3-methylpiperazin-1-yl)pyridin-3-yl]-4-isopropylbenzenesulfonamide hydrochloride from Example 13.4 were dissolved in 10 ml of ethyl acetate, after which 10 mg of palladium on active charcoal (10%) were added and the mixture was stirred overnight at room temperature under a hydrogen atmosphere. After that, the catalyst was filtered off and the filtrate was evaporated down to dryness. After 1 ml of dichloromethane had been added to the resulting residue, diethyl ether was slowly added dropwise until the solution became cloudy. The reaction mixture was stirred for 30 minutes and the precipitate which had formed was filtered off with suction. The filtrate was evaporated down to dryness, after which the residue was dissolved in a 1:1 mixture of dichloromethane and diethyl ether and converted into the hydrochloride by adding ethereal hydrochloric acid. 71 mg (63% of theory) of the title compound were obtained.

^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] 10.9 (bs, 1H); 10.0 (s, 1H); 7.8 (d, 1H); 7.6 (d, 2H); 7.4 (d, 2H); 7.3 (d, 1H); 6.9 (d,1 H); 4.2 (m, 2H); 3.6 (m, 1H); 3.4-3.0 (m, 7H); 1.7 (m, 2H); 1.4 (d, 3H); 1.2 (d, 6H); 0.9 (m, 3H).

MS [m+1]: 417 (free base).

Example 14a: 4-Isopropyl-N-{6-[(3S)-methyl-4-propylpiperazin-1-yl]pyridin-3-yl}benzenesulfonamide as free base (S enantiomer)

The preparation was effected in analogy with the preparation of the racemic compound, with enantiomerically pure (2S)-methylpiperazine being used instead of racemic 2-methylpiperazine.

^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] 9.7 (s, 1H); 7.7 (s, 1H); 7.6 (d, 2H); 7.4 (d, 2H); 7.2 (d, 1H); 6.7 (d,1 H); 3.8 (m, 2H); 2.9 (m, 2H); 2.8 (m, 1H); 2.6 (m, 2H); 2.3 (m, 1H), 2.1 (m, 2H); 1.4 (m, 2H); 1.2 (d, 6H); 1.0 (m, 3H); 0.8 (m, 3H).

MS [m+1]: 417 (free base)

Example 15: N-[5-(4-Allylpiperazin-1-yl)pyridin-2-yl]-4-isopropylbenzenesulfonamide hydrochloride

15.1 1-Allyl-4-(6-nitropyridin-3-yl)piperazine

315 mg (2.5 mmol) of N-allylpiperazine were dissolved in 5 ml of toluene under an argon atmosphere. 93 mg (0.1 mmol) of tris-(dibenzylideneacetone)-dipalladium(0) (Pd_2dba_3), 126 mg (0.2 mmol) of 2,2'-bis-(diphenylphosphino)-1,1'-binaphthyl (BINAP), 1.14 g (3.5 mmol) of cesium carbonate and 515 mg (2.54 mmol) of 5-bromo-2-nitropyridine were then added and the mixture was stirred at 120°C, in a microwave oven, for 4 hours. After the reaction mixture had cooled down to room temperature, a saturated aqueous solution of ammonium chloride was added. After that, the aqueous reaction mixture was extracted three times with in each case 50 ml of ethyl acetate. After the organic phase had been dried over sodium sulfate, the drying agent had been filtered off and the solvent had been evaporated down to dryness, the residue was chromatographed through silica gel using ethyl acetate/methanol (4:1), with 304 mg (46% of theory) of the title compound being obtained.

^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] 8.2 (m, 2H); 7.2 (dd, 1H); 5.9 (m, 1H); 5.3 (m, 2H); 3.5 (m, 4H); 3.1 (m, 2H); 2.6 (m, 4H).

MS [m+1]: 249

15.2 5-(4-Allylpiperazin-1-yl)pyridine-2-amine

300 mg (1.21 mmol) of 1-allyl-4-(6-nitropyridin-3-yl)piperazine from Example 15.1 were dissolved in 20 ml of methanol, after which 2.18 g (9.67 mmol) of tin(II) chloride dihydrate were added and the mixture was stirred at 70°C for 2 hours. After the solvent had been evaporated down to dryness, the resulting residue was treated with water and this mixture was made alkaline using a dilute

aqueous solution of sodium hydroxide and extracted with ethyl acetate. The solid which had precipitated out was filtered off with suction. The phases were then separated and the aqueous phase was extracted three times with ethyl acetate. The combined organic phases were dried over sodium sulfate, filtered and evaporated down to dryness, with 183 mg (69% of theory) of the title compound being obtained.

MS [m+1]: 219.

15.3 N-[5-(4-Allylpiperazin-1-yl)pyridin-2-yl]-4-isopropylbenzenesulfonamide hydrochloride

520 mg (2.38 mmol) of 5-(4-allylpiperazin-1-yl)pyridin-2-ylamine and 495 mg (2.26 mmol) of 4-isopropylbenzenesulfonyl chloride were dissolved in 5 ml of tetrahydrofuran at room temperature, after which 1.0 ml (7.15 mmol) of triethylamine was added dropwise and the mixture was stirred at 40-50°C for 6 hours. After the solvent had been evaporated down to dryness, the resulting residue was treated with water and this mixture was made acid using 1N aqueous hydrochloric acid and extracted twice with diethyl ether. The aqueous phase was made alkaline, to pH 9-10, using a 1N aqueous solution of sodium hydroxide and then extracted twice with ethyl acetate. After the combined organic phases had been dried over sodium sulfate, the drying agent had been filtered off and the solvent had been evaporated down to dryness, the resulting residue was chromatographed on silica gel using ethyl acetate. After the solvent had been removed, the resulting residue was brought into solution using a little diethyl ether in dichloromethane and then converted into the hydrochloride using ethereal hydrochloric acid. 415 mg (44% of theory) of the title compound were obtained.

^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] 11.6 (bs, 1H); 7.9 (d, 1H); 7.8 (d, 2H); 7.5 (dd, 1H); 7.4 (d, 2H); 7.1 (d, 1H); 6.0 (m, 1H); 5.5 (m, 2H); 3.7 (m, 4H); 3.4 (m, 2H); 3.1 (m, 4H); 3.0 (m, 1H); 1.2 (d, 6H).

^{13}C-NMR (100 MHz, DMSO-d_6): δ [ppm] 153.3 (C); 144.5 (C); 141.6 (C); 138.4 (C); 134.3 (CH); 127.3 (CH); 127.0 (CH); 126.8 (CH); 124.8 (CH_2); 113.8 (CH); 57.3 (CH_2); 49.6 (CH_2); 45.2 (CH_2); 33.3 (CH); 23.4 (CH_3).

MS [m+1]: 401.

Example 16: N-[2-(4-Allylpiperazin-1-yl)pyrimidin-5-yl]-4-isopropylbenzenesulfonamide

16.1 2-(4-Allylpiperazin-1-yl)-5-nitropyrimidine

114 mg (2.38 mmol) of 50% sodium hydride were added, under a nitrogen atmosphere and while cooling with ice, to a solution of 273 mg (2.17 mmol) of N-allylpiperazine in 5 ml of dimethylformamide. After 30 minutes, a solution of 440 mg (2.17 mmol) of 2-(methylsulfone)-5-nitropyrimidine in 5 ml of dimethylformamide was added dropwise to the reaction mixture. After 10 minutes, 70 ml of water were added and the reaction mixture was extracted twice with in each case 50 ml of ethyl acetate. After the combined organic phases had been dried over sodium sulfate, the drying agent had been filtered off and the solvent had been evaporated to dryness, 535 mg (99% of theory) of the title compound were obtained.

^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] 9.0 (s, 2H); 5.8 (m, 1H); 5.2 (m, 2H); 4.0 (m, 4H); 3.1 (m, 2H); 2.5 (m, 4H).

MS [m+1]: 250.

16.2 2-(4-Allylpiperazin-1-yl)pyrimidine-5-amine

3.84 g (17.0 mmol) of tin(II) chloride dihydrate were added to a solution of 530 mg (2.13 mmol) of 2-(4-allylpiperazin-1-yl)-5-nitropyrimidine from Example 16.1 in 20 ml of methanol and, after that, the reaction mixture was heated at reflux for 1 hour. After the solvent had been evaporated to dryness, the residue was treated with saturated aqueous sodium chloride solution and then made alkaline using dilute aqueous sodium hydroxide solution. After that, the aqueous reaction mixture was extracted with ethyl acetate. The solid which had precipitated out was filtered off with suction. The phases were then separated and the aqueous phase was extracted in each case twice with ethyl acetate and dichloromethane. After the combined organic phases had been dried over sodium sulfate, the drying agent had been filtered off and the solvent had been evaporated down to dryness, 220 mg (46% of theory) of the title compound were obtained.

16.3 N-[2-(4-Allylpiperazin-1-yl)pyrimidin-5-yl]-4-isopropylbenzenesulfonamide

216 mg (0.98 mmol) of 2-(4-Allylpiperazin-1-yl)pyrimidin-5-ylamine from Example 16.2 and 215 mg (0.98 mmol) of 4-isopropylbenzenesulfonyl chloride were dissolved in 20 ml of tetrahydrofuran at room temperature, after which 0.4 ml (3.0 mmol) of triethylamine was added dropwise and the mixture was stirred at room temperature overnight. After the solvent had been evaporated down to dryness, water was added to the resulting residue. The aqueous reaction mixture

was made acid using 1N aqueous hydrochloric acid and extracted twice with diethyl ether. The aqueous phase was made alkaline to pH 9-10, using a 1N solution of sodium hydroxide and then extracted three times with diethyl ether. The combined organic phases were dried over sodium sulfate. The residue which was obtained after filtering off the drying agent and evaporating the solvent down to dryness was thoroughly stirred with a mixture composed of heptane and diethyl ether, filtered off with suction and dried, with 71 mg (18% of theory) of the title compound being obtained.

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] 8.0 (s, 2H); 7.7 (d, 2H); 7.3 (d, 2H); 6.2 (bs, 1H); 5.9 (m, 1H); 5.2 (m, 2H); 3.8 (m, 4H); 3.1 (m, 2H); 3.0 (m, 1H); 2.5 (m, 4H); 1.3 (d, 6H).

MS [m+1]: 402.

Example 17: 4-Isopropyl-N-[2-(4-propylpiperazin-1-yl)pyrimidin-5-yl]benzenesulfonamide hydrochloride

70 mg (0.17 mmol) of N-[2-(4-allylpiperazin-1-yl)pyrimidin-5-yl]-4-isopropylbenzenesulfonamide from Example 16.3 were dissolved in 30 ml of ethyl acetate, after which 10 mg of palladium on active charcoal (10%) were added and the mixture was stirred at room temperature for 2 hours under a hydrogen atmosphere. The catalyst was then filtered off and the filtrate was concentrated by evaporation. The residue was brought into solution using 25 ml of diethyl ether and converted into the hydrochloride with ethereal hydrochloric acid, resulting in 58 mg (76% of theory) of the title compound being obtained.

^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] 11.0 (bs, 1H); 10.0 (s, 1H); 8.1 (s, 2H); 7.7 (d, 2H); 7.5 (d, 2H); 4.6 (m, 2H); 3.5 (m, 2H); 3.4 (m, 2H); 3.0 (m, 5H); 1.7 (m, 2H); 1.3 (d, 6H); 0.9 m, 3H).

MS [m+1]: 404 (free base).

Example 18: N-[6-(4-Allylpiperazin-1-yl)pyrimidin-4-yl]-4-isopropylbenzenesulfonamide

18.1 N-(6-Chloropyrimidin-4-yl)-4-isopropylbenzenesulfonamide

996 mg (5.0 mmol) of isopropylbenzenesulfonamide were dissolved in 20 ml of dimethyl sulfoxide, after which 288 mg (6.0 mmol) of 50% sodium hydride were added and the mixture was stirred at room temperature for 30 minutes. 819 mg (5.5 mmol) of 4,6-dichloropyrimidine were then added and the reaction mixture was stirred overnight at room temperature. Subsequently, the mixture was heated at 90°C for 3 hours and, after that, stirred at 120°C, in a microwave oven, for 30 minutes. After the reaction mixture had cooled down to room temperature,

it was diluted with 150 ml of water, neutralized with citric acid and extracted three times with diethyl ether. The residue, which was obtained after drying with sodium sulfate and after removing the solvent, was dissolved in 100 ml of diethyl ether and extracted with an aqueous solution of sodium hydrogen carbonate. The aqueous phase was acidified and extracted with diethyl ether. The organic phase was dried, filtered and evaporated down to dryness, with 440 mg (28% of theory) of the title compound being obtained.

MS [m+1]: 312.

18.2 N-[6-(4-Allylpiperazin-1-yl)pyrimidin-4-yl]-4-isopropylbenzenesulfonamide

430 mg (1.38 mmol) of N-(6-chloropyrimidin-4-yl)-4-isopropylbenzenesulfonamide from Example 18.1 were dissolved in 3 ml of dimethyl sulfoxide, after which 1.74 g (13.79 mmol) of N-allylpiperazine were added and the mixture was stirred overnight. Subsequently, the reaction mixture was stirred at 100°C, in a microwave oven, for 45 minutes. After the reaction mixture had cooled down to room temperature, it was diluted with 50 ml of water. After that, the aqueous reaction mixture was extracted with 50 ml of ethyl acetate and the precipitate was filtered off with suction, with 190 mg (34% of theory) of the title compound being obtained.

^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] 8.4 (s, 1H); 7.8 (d, 2H); 7.3 (d, 2H); 6.1 (s, 1H); 5.9 (m, 1H); 5.2 (m, 2H); 3.6 (m, 4H); 3.0 (m, 3H); 2.5 (m, 4H); 1.3 (d, 6H).

MS [m+1]: 402.

Example 19: N-[2-(4-Allylpiperazin-1-yl)pyridin-5-yl]-4-bromobenzenesulfonamide hydrochloride

The preparation was effected in analogy with Example 1.3, with 4-bromobenzenesulfonyl chloride being used instead of 4-isopropylbenzenesulfonyl chloride. The reaction product which was obtained was converted into the hydrochloride using ethereal hydrochloric acid, resulting in 398 mg of the title compound.

MS [m+1]: 436/438

Example 20: N-[6-(4-Allylpiperazin-1-yl)pyridin-3-yl]-4-cyclopropylbenzenesulfonamide

398 mg (0.84 mmol) of N-[6-(4-allylpiperazin-1-yl)pyridin-3-yl]-4-bromobenzenesulfonamide from Example 19, 101 mg (1.18 mmol) of cylcopropylboronic acid, 676 mg (3.19 mmol) of K_3PO_4 and 26 mg (0.09 mmol) of tricyclohexylphosphine were dissolved in 4 ml of toluene and 0.2 ml of water under a

nitrogen atmosphere. 10 mg (0.04 mmol) of palladium(II) acetate were then added and the mixture was stirred at 100°C, in a microwave oven, for one hour. After the solvent had been evaporated down to dryness, the resulting residue was treated with water and the mixture was then extracted with ethyl acetate. Because the phases only separated poorly, the finely divided solid was filtered off. The aqueous phase was extracted twice with ethyl acetate. After the combined organic phases had been dried over sodium sulfate and the solvent had been filtered and evaporated down to dryness, the resulting residue was purified by column chromatography.

MS [m+1]: 399

The compounds of the following examples 21 to 40 were prepared in analogous manner:

Example 21: 4-Isopropyl-N-[2-(4-propylpiperazin-1-yl)pyridin-3-yl]-benzenesulfonamide hydrochloride

MS [m+1]: 403 (free base).

Example 22: 4-Isopropyl-N-[2-(3,5-dimethyl-4-propylpiperazin-1-yl)pyridin-3-yl]benzenesulfonamide trifluoroacetate

MS [m+1]: 431 (free base).

Example 23: N-[2-(4-Allyl-3-methylpiperazin-1-yl)pyridin-3-yl]-4-trifluoromethylbenzenesulfonamide hydrochloride

MS [m+1]: 441 (free base).

Example 24: *N*-[6-(4-Allyl-3,5-dimethylpiperazin-1-yl)pyridin-3-yl]-4-isopropylbenzenesulfonamide hydrochloride

MS [m+1]: 429 (free base)

Example 25: *N*-[6-(4-Allyl-3,5-dimethylpiperazin-1-yl)pyridin-3-yl]-4-trifluoromethylbenzenesulfonamide hydrochloride

MS [m+1]: 455 (free base)

Example 26: *N*-[6-(4-Allylpiperazin-1-yl)pyridin-3-yl]-4-trifluoromethylbenzenesulfonamide

MS [m+1]: 427

Example 27: 4-Bromo-*N*-[6-(4-propylpiperazin-1yl)pyridin-3-yl]-benzenesulfonamide

MS [m+1]: 439/441

Example 28: 4-Chloro-*N*-[6-(4-propylpiperazin-1yl)pyridin-3-yl]-benzenesulfonamide

MS [m+1]: 395

Example 29: 4-Isopropyl-*N*-[6-(5-propyl-2,5-diazabicyclo[2.2.1]hept-2-yl)pyridin-3-yl]-benzenesulfonamide hydrochloride

MS [m+1]: 415 (free base)

Example 30: *N*-[6-(5-Allyl-2,5-diazabicyclo[2.2.1]hept-2-yl)pyridin-3-yl]-4-isopropylbenzenesulfonamide hydrochloride

MS [m+1]: 413 (free base)

Example 31: *N*-[6-(4-Propylpiperazin-1-yl)pyridin-3-yl]-4-vinylbenzenesulfonamide hydrochloride

MS [m+1]: 387 (free base)

Example 32: *N*-{6-[4-(3-Fluoropropyl)piperazin-1-yl]pyridin-3-yl}-4-isopropylbenzene-sulfonamide hydrochloride

MS [m+1]: 421 (free base)

Example 33: 4-Isopropyl-*N*-[6-(4-prop-2-yn-1-ylpiperazin-1-yl)pyridin-3-yl]-benzenesulfonamide hydrochloride

MS [m+1]: 399 (free base)

Example 34: 4-Ethyl-*N*-[6-(4-propylpiperazin-1-yl)pyridin-3-yl]-benzenesulfonamide hydrochloride

MS [m+1]: 389 (free base)

Example 35: *N*-[6-(4-Allylpiperazin-1-yl)pyridin-3-yl]-4-chlorobenzenesulfonamide hydrochloride

MS [m+1]: 393 (free base)

Example 36: 4-Isopropyl-*N*-(4-methyl-6-piperazin-1-ylpyridin-3-yl)-benzenesulfonamide hydrochloride

MS [m+1]: 375 (free base)

Example 37: *N*-[6-(4-Allylpiperazin-1-yl)-4-methylpyridin-3-yl]-4-isopropylbenzene-sulfonamide hydrochloride

MS [m+1]: 415 (free base)

Example 38: 4-Isopropyl-*N*-[4-methyl-6-(4-propylpiperazin-1-yl)pyridin-3-yl]-benzene-sulfonamide hydrochloride

MS [m+1]: 417 (free base)

Example 39: *N*-[4-Methyl-6-(4-propylpiperazin-1-yl)pyridin-3-yl]-4-vinylbenzene-sulfonamide hydrochloride

MS [m+1]: 401 (free base)

Example 40: *N*-[6-(4-Butylpiperazin-1-yl)pyridin-3-yl]-4-isopropylbenzenesulfonamide hydrochloride

MS [m+1]: 417 (free base)

Example 41: *N*-{6-[(3*S*)-4-Ethyl-3-methylpiperazin-1-yl]pyridin-3-yl}-4-isopropylbenzenesulfonamide hydrochloride

MS [m+1]: 403 (free base)

Examples of galenic administration forms

A) Tablets

Tablets of the following composition are pressed on a tablet press in the customary manner:

40 mg of substance from Example 2
120 mg of corn starch
13.5 mg of gelatin
45 mg of lactose
2.25 mg of Aerosil® (chemically pure silicic acid in submicroscopically fine dispersion)
6.75 mg of potato starch (as a 6% paste)

B) Sugar-coated tablets

20 mg of substance from Example 2
60 mg of core composition
70 mg of saccharification composition

The core composition consists of 9 parts of corn starch, 3 parts of lactose and 1 part of 60:40 vinylpyrrolidone/vinyl acetate copolymer. The saccharification composition consists of 5 parts of cane sugar, 2 parts of corn starch, 2 parts of calcium carbonate and 1 part of talc. The sugar-coated tablets which had been prepared in this way are subsequently provided with a gastric juice-resistant coating.

Biological investigations – receptor binding studies:

The substance to be tested was either dissolved in methanol/Chremophor® (BASF-AG) or in dimethyl sulfoxide and then diluted with water to the desired concentration.

Dopamine D_3 receptor:

The assay mixture (0.250 ml) was composed of membranes derived from ~ 10^6 HEK-293 cells possessing stably expressed human dopamine D_3 receptors, 0.1 nM [^{125}I]-iodosulpride and incubation buffer (total binding) or, in addition, test substance (inhibition curve) or 1μM spiperone (nonspecific binding). Each assay mixture was run in triplicate.

The incubation buffer contained 50 mM tris, 120 mM NaCl, 5 mM KCl, 2 mM $CaCl_2$, 2 mM $MgCl_2$ and 0.1% bovine serum albumin, 10 μM quinolone and 0.1% ascorbic acid (prepared fresh daily). The buffer was adjusted to pH 7.4 with HCl.

Dopamine D_{2L} receptor:

The assay mixture (1 ml) was composed of membranes from ~ 10^6 HEK-293 cells possessing stably expressed human dopamine D_{2L} receptors (long isoform) and 0.01 nM [^{125}I] iodospiperone and incubation buffer (total binding) or, in addition, test substance (inhibition curve) or 1μM haloperidol (nonspecific binding). Each assay mixture was run in triplicate.

The incubation buffer contained 50 mM tris, 120 mM NaCl, 5 mM KCl, 2 mM $CaCl_2$, 2 mM $MgCl_2$ and 0.1% bovine serum albumin. The buffer was adjusted to pH 7.4 with HCl.

Measurement and analysis:

After having been incubated at 25°C for 60 minutes, the assay mixtures were filtered through a Wathman GF/B glass fiber filter under vacuum using a cell collecting device. The filters were transferred to scintillation viols using a filter transfer system. After 4 ml of Ultima Gold® (Packard) have been added, the samples were shaken for one hour and the radioactivity was then counted in a Beta-Counter (Packard, Tricarb 2000 or 2200CA). The cpm values were converted into dpm using a standard quench series and the program belonging to the instrument.
The inhibition curves were analyzed by means of iterative nonlinear regression analysis using the Statistical Analysis System (SAS) which is similar to the "LIGAND" program described by Munson and Rodbard.

In these tests, the compounds according to the invention exhibit very good affinities for the D_3 receptor (< 100 nM, frequently < 50 nM) and bind selectively to the D_3 receptor. The results of the binding tests are given in Table 1.

Table 1:

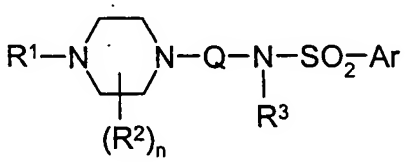
Example	K_i (D_3) [nM]	Selectivity vs. D_2L
1	3.0	232
2	5.5	25
3	5.9	15
5	11.4	108
6	9.7	169
7	11.4	68
10	7.5	93
11	6.2	77
13	3.6	131
13a	2.7	96
14	2.5	81

Example	K_i (D_3) [nM]	Selectivity vs. D_2L*
14a	1.5	184
16	3.8	131
17	8.2	148
19	36.9	91
22	21.9	22
24	25.0	47
27	21.4	55
28	25.3	67
29	16.9	31
30	11.1	17
31	14.0	96
32	17.0	74
34	9.6	73
35	26.6	51
36	5.4	50
37	2.7	86
38	17.2	22
39	34.6	30

* $K_i(D_3)/K_i(D_{2L})$

Patent claims:

1. An N-[(piperazinyl)hetaryl]arylsulfonamide compound of the general formula I



(I)

in which

Q is a bivalent, 6-membered heteroaromatic radical which possesses 1 or 2 N atoms as ring members and which optionally carries one or two substituents R^a which is/are selected, independently of each other, from halogen, CN, NO_2, CO_2R^4, COR^5, C_1-C_4-alkyl and C_1-C_4-haloalkyl;

Ar is phenyl or a 6-membered heteroaromatic radical which possesses 1 or 2 N atoms as ring members and which optionally carries one or two substituents R^b, which is/are selected from halogen, NO_2, CN, CO_2R^4, COR^5, C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_6-cycloalkyl, C_3-C_6-cycloalkyl-C_1-C_4-alkyl and C_1-C_4-haloalkyl, with it also being possible for two radicals R^b which are bonded to adjacent C atoms of Ar to be together C_3-C_4-alkylene;

n is 0, 1 or 2;

R^1 is hydrogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_3-C_6-cycloalkyl, C_3-C_6-cycloalkyl-C_1-C_4-alkyl, C_1-C_4-hydroxyalkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_3-C_4-alkenyl or C_3-C_4-alkynyl;

R^2 is C_1-C_4-alkyl or, together with R^1, is C_2-C_5-alkylene or, in the case of n = 2, the two radicals R^2 can together be C_1-C_4-alkylene;

R^3 is hydrogen or C_1-C_4-alkyl;

R^4 is C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_2-C_4-alkenyl C_3-C_6-cycloalkyl, C_3-C_6-cycloalkyl-C_1-C_4-alkyl, phenyl or benzyl; and

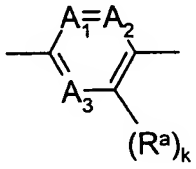
R^5 is hydrogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_2-C_4-alkenyl C_3-C_6-cycloalkyl, C_3-C_6-cycloalkyl-C_1-C_4-alkyl, phenyl or benzyl;

the N-oxides thereof and the physiologically tolerated acid addition salts of these compounds;

with the exception of the compounds: 4-methyl-N-[6-(4-methylpiperazin-1-yl)pyridin-3-yl)benzenesulfonamide and 4-chloro-N-[6-(4-methylpiperazin-1-yl)pyridin-3-yl)benzenesulfonamide.

2. The compound as claimed in claim 1, in which the piperazine ring is bonded to the heteroaromatic radical Q in the para position in relation to the group $N(R^3)$-SO_2-Ar.

3. The compound as claimed in one of the preceding claims, in which Q is a radical of the formula



in which A_1, A_2 and A_3 are, independently of each other, N or CH, one or two of the variables A_1, A_2 and A_3 can also be C-R^a, k = 0 or 1 and R^a is selected from halogen, C_1-C_4-alkyl and C_1-C_4-haloalkyl, with A_1, A_2 and A_3 not simultaneously being N or simultaneously being selected from CH and C-R^a.

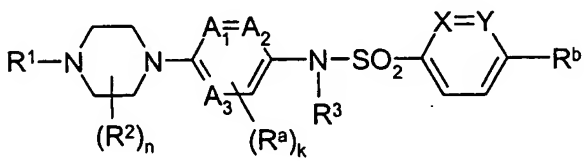
4. The compound as claimed in claim 3, in which Q is pyridin-2,5-diyl which carries the piperazine radical in the 2 position.

5. The compound as claimed in one of the preceding claims, in which the radical Ar carries a substituent R^b in the para position and, where appropriate, a further substituent R^b in the meta position or in the ortho position, in each case based on the binding site of the sulfonamide group.

6. The compound as claimed in one of the preceding claims, in which Ar is phenyl or pyridyl, which radicals possess, where appropriate, one or 2 R^b substituents.

7. The compound as claimed in one of the preceding claims, in which R^1 is different from hydrogen and methyl.

8. The compound as claimed in claim 1 of the general formula Ia



(Ia)

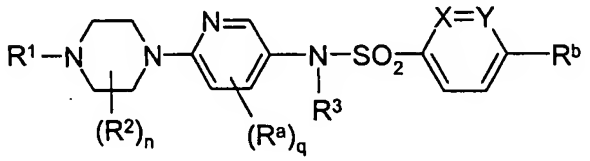
in which n, R^1, R^2, R^3, R^a and R^b have the meanings given in claim 1 and in which either

A_1, A_2 and A_3 are, independently of each other, N or CH and one or two of the variables A_1, A_2 and A_3 can also be C-R^a, with A_1, A_2 and A_3 not simultaneously being N or simultaneously being selected from CH and C-R^a,

X and Y are selected from CH, C-$R^{b'}$ and N, in which $R^{b'}$ is halogen, methyl, CN, difluoromethyl or trifluoromethyl, with X and Y not simultaneously being N or simultaneously being C-$R^{b'}$, and

k is 0 or 1.

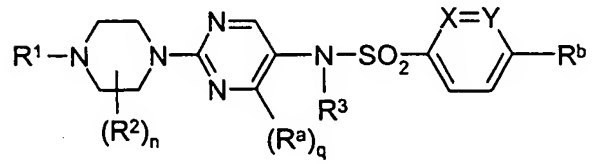
9. The compound as claimed in claim 8 of the general formula Ia.1



(Ia.1)

in which n, X, Y, R^1, R^2, R^3, R^a and R^b have the meanings given in claim 8 and q is 0, 1 or 2.

10. The compound as claimed in claim 8 of the general formula Ia.2



(Ia.2)

in which n, X, Y, R^1, R^2, R^3, R^a and R^b have the meanings given in claim 8 and q is 0, 1 or 2.

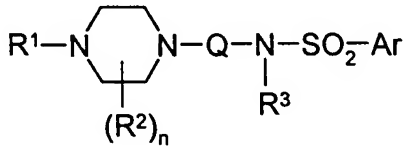
11. The compound as claimed in claim 8, in which k = 0, with A_1, A_2 and A_3 being, independently of each other, N or CH and A_1, A_2 and A_3 not simultaneously being N or simultaneously being CH.

12. The compound as claimed in one of claims 8 to 11, in which n is 0 or 1 and, in the case of n = 1, R^2 is bonded to the C atom of the piperazine ring which is adjacent to the group R^1-N and is a methyl group having the S configuration.

13. A pharmaceutical composition which comprises at least one N-[(piperazinyl)hetaryl]arylsulfonamide compound as claimed in one of claims 1 to 10 and/or at least one physiologically tolerated acid addition salt of I and/or an N-oxide of I,

where appropriate together with physiologically acceptable carriers and/or auxiliary substances.

14. The use of at least one N-[(piperazinyl)hetaryl]arylsulfonamide compound of the formula I



(I)

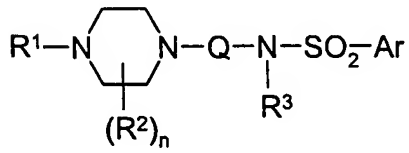
in which Q, Ar, n, R^1, R^2 and R^3 have the previously mentioned meanings, of the N-oxides thereof and of the physiologically tolerated acid addition salts thereof for producing a pharmaceutical composition for treating diseases which respond to influencing by dopamine D_3 receptor antagonists or dopamine D_3 agonists.

15. The use as claimed in claim 14 for treating diseases of the central nervous system.

16. The use as claimed in claim 14 for treating kidney function disturbances.

Abstract

The invention relates to N-[(piperazinyl)hetaryl]arylsulfonamide compounds of the general formula I



(I)

in which

Q is a bivalent, 6-membered heteroaromatic radical which possesses 1 or 2 N atoms as ring members and which optionally carries one or two substituents R^a which is/are selected, independently of each other, from halogen, CN, NO_2, CO_2R^4, COR^5, C_1-C_4-alkyl and C_1-C_4-haloalkyl;

Ar is phenyl or a 6-membered heteroaromatic radical which possesses 1 or 2 N atoms as ring members and which optionally carries one or two substituents R^b, which is/are selected from halogen, NO_2, CN, CO_2R^4, COR^5, C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_6-cycloalkyl, C_3-C_6-cycloalkyl-C_1-C_4-alkyl and C_1-C_4-haloalkyl, with it also being possible for two radicals R^b which are bonded to adjacent C atoms of Ar to be together C_3-C_4-alkylene;

R^1 is hydrogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_3-C_6-cycloalkyl, C_3-C_6-cycloalkyl-C_1-C_4-alkyl, C_1-C_4-hydroxyalkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_3-C_4-alkenyl or C_3-C_4-alkynyl;

with the radicals n, R^1, R^2, R^3, R^4 and R^5 having the meanings given in the patent claims, to the N-oxides and to the physiologically tolerated acid addition salts of these compounds and to pharmaceutical compositions which comprise at least one N-[(piperazinyl)hetaryl]arylsulfonamide compound as claimed in one of claims 1 to 10 and/or at least one physiologically tolerated acid addition salt of I and/or an N-oxide of I, where appropraite together with physiologically accpetable carriers and/or auxiliary substances for treating diseases which respond to influencing by dopamine D_3 receptor antagonists or agonists, in particular for treating diseases of the central nervous system and disturbances of kidney function.